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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service • National Institutes of Health • National Cancer Institute

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PREVALENCE OF GI CANCER IN HUMAN POPULATIONS

1. EARLY IDENTIFICATION OF INDIVIDUALS AT INCREASED RISK FOR CANCER OF THE LARGE INTESTINE. PART I: DEFINITION OF HIGH RISK POPULATIONS.

Lipkin M, Winawer SJ, Sherlock P

Gastroenterology Service, Dept. Medicine, Memorial Sloan-Kettering Cancer Inst., New York, NY

Clin Bull; 11(1):13-21 1981

The major population groups at increased risk for cancer of the large intestine are described. A comprehensive registry of individuals and familial groups includes those with: familial polyposis, Peutz-Jegher's syndrome, juvenile polyposis, familial colon cancer without polyposis, multiple cancers including colorectal, single and multiple sporadic colorectal adenomas, primary colorectal cancer, ulcerative colitis, and Crohn's disease. Familial polyposis, an autosomal dominant genetic defect affecting each generation, is expressed phenotypically 80% of the time. Gardner's syndrome is a variant of familial polyposis with lower incidence (1/14,000 births). Related inherited cancers are Turcot syndrome and Peutz-Jegher's syndrome (where the carcinoma is believed to arise from adenomas). In juvenile polyposis, most cases have been solitary rather than familial; both noncancerous polyps, adenomatous tumors, and tumors exhibiting combined characteristics have been observed. Other forms of gastrointestinal cancer may occur with hereditary predisposition; criteria identifying a familial syndrome are 1) increased numbers of all types of adenocarcinomas, 2) early age of cancer development, 3) tendency to multiple primary malignant neoplasms, and 4) segregation ratios consistent with autosomal dominant mode of inheritance. Children of affected parents suffer an approx 50% risk of developing colorectal cancer. Risk factors are identified for the remaining, less demonstrably heritable, registry categories. An estimated 5% of adenomas become malignant; the development of villous characteristics in the adenomas is associated with increased frequency of malignancy. The life-time cancer risk of patients with ulcerative colitis is approx 57%. (34 Refs)

2. GEOGRAPHICAL VARIATIONS IN CANCER INCIDENCE IN TWO URBAN POPULATIONS IN INDIA.

Jussawalla DJ, Yeole BB, Natekar MV, Rajagopalan TR

Bombay Cancer Registry, Indian Cancer Society, Parel, Bombay 400 012, India

Indian J Cancer; 18(2):91-98 1981

The variation in cancer incidence between the populations of Greater Bombay and Poona City was investigated by age, sex, and site. Both age adjusted and truncated rates are reported and a simplified statistical method was used for testing the variations. Between 1972 and 1974, there were 12,969 new cancer cases in Bombay and 2,670 new cases in Poona City. The sex distribution showed many more males than females in Bombay (7,428 vs 5,541) than in Poona City (1,346 vs 1,324). In both areas cancer incidence increased sharply with age. In Bombay, more cancers of the tongue, pharynx, esophagus, and lung were seen. while in Poona City, more cancers of the stomach, buccal mucosa, rectum, and penis in males, and stomach, breast, uterus and cervix in females were seen. These differences are attributed to differences in the environmental, geographical and demographic status of these two cities. (10 Refs)

3. THE CENTRAL CANCER REGISTRY OF THE HEALTH COMMISSION OF NEW SOUTH WALES.

McEwin R, Ford J, Goulston K

Health Commission of New South Wales, New South Wales, Australia

Cancer Forum; 5(1):19-24 1981

A review of the New South Wales (NSW) Cancer Registry, a unit of the Health Commission of New South Wales, is presented. The registry has been in operation since 1972 with the following aims: to delineate the nature and extent of cancer in NSW, to provide information which can be used in the control and prevention of cancer, to explore and determine the etiological aspects of cancer, and to describe the natural history of all types of cancer. The 1976 data show that in NSW, the leading sites of cancer in males were lung and colon and rectum; in females, they were breast and colon/rectum. The commonest cancer was skin cancer, but data are not collected for squamous and basal cell carcinoma of the skin. The data in the registry are presented as cross-tabulations for new cases and deaths, by age and sex, related to cancer sites, subsites, and cell types: for the State, Health Regions, Local Government areas, and for various ethnic groups. Applications of the data in the registry are discussed. (2 Refs)

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN GI CARCINOGENESIS

4. EPIDEMIOLOGY OF ASBESTOS-RELATED TUMORS.

Newhouse M

London Sch. Tropical Medicine and Hygiene, Keppel St. (Gower St.), London WC1 E7HT, England

Semin Oncol; 8(3):250-257 1981

Tumors shown to be related to the exposure of various asbestos dusts include mesothelioma of the pleura and peritoneum, a rare tumor in the general population but an important cause of death in particular asbestos workers; bronchogenic carcinoma; and possibly gastrointestinal tumors and cancer of the larynx. A case control study of patients dying of mesothelioma at The London Hospital since 1916 revealed that in addition to occupational exposure, domestic contact with dust was also important in the pathogenesis of mesothelioma. It was shown that increasing severity of exposure and increasing length of exposure were associated with an increased death rate from mesothelioma. Factors influencing the incidence of mesothelioma are the concentration of dust to which the workers were exposed, the length of time exposed, and the predominant type of asbestos fibers used. A synergistic effect of cigarette smoking and asbestos exposure on lung cancer has particularly important implications for asbestos workers. A strong anticancer antismoking campaign and careful screening of asbestos workers for lung cancer and mesothelioma are advocated. Other asbestos-related tumors, gastrointestinal cancers and cancer of the larynx warrant further investigation to define the relative risk and to determine what, if any, other cocarcinogenic factors may be involved. (37 Refs)

DIETARY AND DIGESTIVE FACTORS IN GI CARCINOGENESIS

5. ENDOGENOUS CARCINOGENS.

Hill MJ
Bacterial Metabolism Res. Lab., Central Public Health Lab., London, England
Practitioner; 225(1356):803-804,807-809 1981

Estradiol is a potential endogenous carcinogen. Consuming a high fat/high energy diet, by increasing circulating estrogen levels and estrogen receptor activity, may increase the risk of carcinogenesis in estrogen-dependent tissues (breast, endometrium, possibly ovary). The role of cholesterol in carcinogenesis is not yet clear. The author's studies showed no relationship between fecal cholesterol levels and the risk of intestinal cancer in case-control studies. Some of the numerous urinary metabolites of tryptophan seem to be related to non-industrial bladder cancer. Intestinal bacteria can derive carcinogenic substances (ethionine, phenol, p-cresol, N-nitroso compounds, bile acid metabolites, etc) from dietary components and convert exogenous chemicals (eg, polycyclic aromatic hydrocarbons) to proximate carcinogens. It is relatively easy to determine which carcinogens might be produced under ideal conditions, but there is limited information on which carcinogens are actually produced in vivo, and very little information regarding their importance. (27 Refs)

6. ROLE OF DIETARY FIBER IN DIVERTICULAR DISEASE AND COLON CANCER.

Talbot JM
Life Sciences Res. Office, Federation of American Societies for Experimental Biology, Bethesda, MD, 20014
Fed Proc; 40(9):2337-2342 1981

This paper reviews recent research on the characterization, properties, and definition of dietary fiber as well as its possible role in colonic carcinogenesis and diverticulosis. Despite progress in analytic methods and characterization, an accepted definition and terminology for fiber are lacking as is an accurate, rapid method for measurement of total dietary fiber or fiber in foods. Mechanisms of effects of fiber in the gut and the significance of interactions between fiber, nutrients, gut flora and associated metabolites, and enteric secretions are unclear. Epidemiologic and experimental data indicate an increased risk of diverticular disease and colonic cancer with low-fiber intakes; however, genetic, environmental, cultural, dietary, and other variables were often uncontrolled in the epidemiologic studies. Thus, conclusive evidence for a causal relationship between low intake of fiber and diverticulosis or colonic cancer is not available, and the question whether fiber protects against human colonic cancer and/or diverticulosis is not completely resolved. Clinical trials in which symptomatic diverticular disease was treated with supplementary dietary fiber have generally had favorable results. Numerous specific questions require additional study before a role for dietary fiber in the prevention of human colonic diverticulosis and cancer of the colon can be established. Suggestions for possible future investigation are provided. (Author abstract) (61 Refs)

7. SMOKING, DRINKING, EATING, AND SEX. SOME PRACTICAL ASPECTS OF PREVENTING DEATHS FROM CANCER.

Cust G
Trent Regional Health Authority, Trent, England
Practitioner; 225(1356):853-856 1981

Prevention of death from cancer is linked with alterations in smoking, drinking, eating, and sexual habits. For smoking, risk reduction is related to abstinence, using filter cigarettes, reducing alcohol consumption concurrently with cigarette smoking, and avoiding environments which contain cigarette smoke. Alcohol appears to have a synergistic effect with other substances in increasing the risk of cancer. Particular dietary etiologies of cancer have not been clearly shown, but a high proportion of meat, fat, and refined carbohydrate relative to fiber has been suggested as a cause of colon cancer. Screening programs for cervical cancer are thought to be the best method for reducing risk and death from cervical carcinoma. (7 Refs)

8. DIET AND LAXATIVES: RISK FACTORS FOR CANCER OF THE COLON? (MEETING ABSTRACT).

Bevilacqua M, Giongo F
Divisione Lungadegenza Riabilitativa di Patologia Medica, Ospedale L Sacco, Milan, Italy
Tumori; 67(2,SupplA):61 1981

The discovery of an increased amount of nitrogen, lipids, cholesterol, bile acids and sterols in the feces of a population predisposed to cancer of the colon, with an increased tendency to production of potentially carcinogenic metabolites (such as desoxycholic acid) combined with the presence of large numbers of anaerobic bacteria (especially bacteroids, which are active in degrading the cholate of bile acids into desoxycholate) raises the suspicion that a cocausal role, if not causal, can be attributed to certain foods in the diet which is of considerable importance: increased consumption of protein (meat especially beef, which contains high fat levels); increased fat consumption (which alter not only the concentration of bile acids and cholesterol metabolites, but also the activity of intestinal bacterial microflora); increased consumption of carbohydrates, especially sugars; increased oxidase production (fecal bacterial 7-alpha-dehydroxylase changes the primary bile acids, cholic and chenodeoxycholic, into secondary bile acids); low roughage in the diet (which tends to reduce intestinal transit time and inhibit degradation of cholates and bile acids). As for laxatives and purgatives, the discussion must be confined to their composition more than their effect on intestinal motility (on which the jury is still out): various commercial preparations contain bile salts and/or extracts (from 20 to 150 mg/dose). (no Refs) (In ITA)

OTHER ETIOLOGIC FACTORS IN GI CARCINOGENESIS

9. PSYCHOSOCIAL FACTORS IN THE ETIOLOGY OF CANCER.

Morrison FR
University of California, Berkeley, CA
Diss Abstr Int (B); 42(1):155-B 1981

The study utilized files maintained on approx 15,000 men and women former students of the University of Pennsylvania.

Data on 'potential cause' was collected at college entrance in 1931-1940, 36 to 45 yr in advance of 'observed effect' --the development of or death from cancer. The results of this investigation provide no evidence that psychological characteristics measured in youth are predictive of all cancers later in life. No differences in response to 71 psychophysiological items were found among former students who died of cancer, those who died of other causes and those alive. Relative risks based on death rates calculated separately for those who answered 'yes' and those who answered 'no' to 15 cancer of those who died of any other cause in either men or women. Further, response to these psychological items was not associated with a significantly increased risk for those who died of lung or pancreatic cancer in men, and breast cancer in women. No elevated risk, based on response to the psychological items, was noted in men with colorectal cancer or women with breast cancer who were alive in 1976. Elevated risks were found only for 34 men who died of colorectal cancer. The patterns of responses in these decedents suggested a group of men who were tense, anxious, and self-conscious with a tendency to translate psychological states into somatic symptoms. The disparity in results for colorectal cancer decedents and those alive with the disease is disquieting, but it is possible that those already dead may constitute a substantially different subgroup among those who develop cancer of the colon or rectum. (no Refs)

10. THE ROLE OF N-NITROSAMINE IN CARCINOGENESIS AT THE URETEROCOLIC ANASTOMOSIS.

Stewart M, Hill MJ, Pugh RC, Williams JP
St. Paul's Hosp., 24 Endell St., London WC2H 9AE, England
Br J Urol; 53(2):115-118 1981

Seven cases of colonic tumors occurring at the ureterocolic anastomosis (UCA) in patients diverted for benign disease are presented and comparisons made with existing literature. There appears to be a definite increase in the incidence of colonic malignancy in patients with this diversion. A theory of carcinogenesis involving bacterial activation of endogenously formed N-nitrosamine is suggested. Preliminary results of rectal urine analysis support this theory in that high concentrations of N-nitrosamine have been found and mutagens demonstrated. (Author abstract) (10 Refs)

11. CHOLECYSTECTOMY AND RIGHT-SIDED COLON CANCER: AN EPIDEMIOLOGICAL STUDY.

Vernick LJ, Kuller LH
(c/o Kuller) Dept. Epidemiology, Graduate Sch. Public Health, Univ. Pittsburgh, Pittsburgh, PA
Lancet; 2(8243):381-383 1981

The relation between prior cholecystectomy and right-sided colon cancer was investigated in a case-control study of 150 patients with histologically confirmed adenocarcinoma of the cecum or ascending colon and of two comparison groups. One comparison group consisted of 150 patients, matched for age, sex, and race, who had histologically confirmed adenocarcinoma of the descending or sigmoid colon and the other of 123 neighborhood controls. Compared with left-sided cancer controls, the right-sided colon cancer cases had a relative risk of 1.87 for colon cancer after cholecystectomy. The relative risk was 1.86 when they were compared with the neighborhood controls. When compared with both control groups relative risk was 1.77, with 95% confidence limits of 0.95 and 3.3 ($p = 0.07$). The increased risk of right-sided colon cancer after cholecystectomy may be associated with changes in biliary metabolism occurring after removal of a gall bladder. (Author abstract) (18 Refs)

12. CHOLECYSTECTOMY AND CARCINOMA OF THE COLON.

Linos DA, O'Fallon WM, Beart RW, Beard CM, Dockerty MB, Kurland LT
Section Publications, Mayo Clinic, Rochester, MN, 55905
Lancet; 2(8243):379-381 1981

After cholecystectomy the concentration of secondary bile acids in the bile increases. These bile acids have been incriminated in the pathogenesis of carcinoma of the colon. Hence the hypothesis that cholecystectomy predisposes to the development of carcinoma of the colon. To test this hypothesis, 1,681 residents of Rochester, Minnesota (460 males and 1,221 females), who underwent cholecystectomy during 1950-69, were followed up. Carcinoma of the colon developed in a higher-than-expected number of patients. However, the association was significant only in females (relative risk 1.7; 95% confidence interval 1.1-2.5) and even stronger for right-sided carcinoma of the colon (relative risk 2.1; 95% confidence interval 1.1-3.6). These data support the hypothesis that cholecystectomy may be a predisposing factor in the development of cancer of the colon in women. (Author abstract) (20 Refs)

13. BILE ACIDS IN THE FECES AND THEIR RELATION TO COLON CANCER: COMPARATIVE STUDIES OF JAPANESE AND AMERICANS (MEETING ABSTRACT).

Takahashi M, Kodama M, Tamura T, Ezaki H, Hoshita T, Cohen BI
Dept. Surgery, Chugoku Rosai Hosp., Kure-shi, Hiroshima Pref. 737-01, Japan
Nippon Geka Gakkai Zasshi; 82(Suppl):168 1981

Feces of Japanese and Americans were examined for sterols and iso-bile acids having a hydroxy group at the 3beta position, since the risk of developing colon cancer is greater in Americans than in Japanese. The concentration of bile acid in the feces was 7.5 +-3.4 mg/g of feces for healthy Americans ($n=16$)and 10.3 +-5.3 mg/g of feces for Americans with colon cancer ($n=12$). On the other hand, the concentration in the feces of healthy Japanese and those with colon cancer was 2.9 +-1.4 ($n=10$) and 3.8 +-0.7 mg ($n=10$), respectively. While the bile of the Americans consisted of only secondary bile acids, that of the healthy Japanese and Japanese with colon cancer was comprised of 33% and 10% primary bile acids, respectively. The percentage of iso-bile acids (isolithocholic acid + isodeoxycholic acid), which are considered to be produced by the intestinal flora, was 33% and 32%, respectively, for the healthy Americans and Americans with colon cancer, while it was 16% and 31%, respectively, for the healthy Japanese and Japanese with colon cancer. When methylnitrosourea (MNU) was injected into the intestines of rats, the percentage of rats which developed colon tumors was 49%, but when MNU was given together with isolithocholic or lithocholic acid, it was 46% and 65%, respectively, only lithocholic acid having a colon cancer-promoting effect. (no Refs) (In JPN)

14. THE MORPHOLOGY AND DYNAMICS OF THE GASTRIC MUCOSA AFTER PARTIAL GASTRECTOMY.

Saukkonen M, Sipponen P, Kekki M
Div. Gastroenterology, Second Dept. Medicine, Univ. Helsinki, SF-00290 Helsinki 29, Finland
Ann Clin Res; 13(3):156-158 1981

The morphology and dynamics of the gastric mucosa were studied in 121 patients with duodenal ulcers who had Billroth II gastrectomies 2, 5, 10, 15, and 20 yr before. Compared with controls, these patients had significantly more intestinal metaplasia, epithelial dysplasia, hyperplasia, and cyst formation around the gastroenterostomy. These changes, in addition to achlorhydria and regurgitation with subsequent bacterial growth and nitrosamine production, are probably related to the pathogenesis of stump carcinoma. (3 Refs)

15. FAMILY BEHAVIOUR OF CHRONIC GASTRITIS.

Varis K
Second Dept. Medicine, Univ. Helsinki, SF-00290 Helsinki 29, Finland
Ann Clin Res; 13(3):123-129 1981

Chronic gastritis can be divided into three topographically and dynamically different subtypes, discernable at the familial level: type A gastritis mucosal alterations predominate in the body area, type B in the antral area, and type AB in the antrum and body. A major factor, 'Factor A,' is involved in the development of severe atrophic gastritis of the body. This factor is an autosomal dominantly inherited factor. While the etiopathogenic backgrounds of type A gastritis without anemia and that of pernicious anemia are identical, complete penetration of the influence of Factor A is necessary for complete or almost complete lack of intrinsic factor secretion. Parietal cell antibodies may be a phenomenon which parallels atrophic gastritis of the body but has no direct causal relationship with it. The etiological factors of these two phenomena are closely associated, but not identical. While a relation between chronic atrophic gastritis to the intestinal type of gastric carcinoma can be demonstrated only at the individual level, chronic atrophic gastritis is related to the diffuse type of gastric carcinoma at the family level, and not at the individual level. (14 Refs)

16. DYNAMIC BEHAVIOUR OF GASTRITIS IN VARIOUS POPULATIONS AND SUBPOPULATIONS.

Kekki M, Villako K
Second Dept. Medicine, Univ. Helsinki, SF-00290 Helsinki 29, Finland
Ann Clin Res; 13(3):119-122 1981

The use of stochastic principles for the description of the dynamics of gastritis on a population level is reviewed. This approach makes it possible to obtain dynamic follow-up data from simple cross-sectional material, and allows a direct comparison of materials with different age distribution. The dynamics of gastritis in both samples of the general population and on a family level are reviewed as are the transition risks of gastritis. In the families of the probands with diffuse type of gastric carcinoma, the mean gastritic score of the relatives correlated with the age of the proband; no such relation was found in the families of the probands with the other types of gastric carcinoma. With the family approach, it was shown that three different family patterns exist: families with gastritis affecting mainly the body or mainly the antral mucosa and those with gastritis involving these two areas almost equally. The latter pattern probably represents the main behavior in the population at large. The application of stochastic mathematics to representative populations or subpopulations allows the yearly risk of the transition of gastritis to the stage next in severity to be calculated. (9 Refs)

17. GASTRIC POLYPS AND GASTRIC CARCINOMA.

Laxen F
Div. Gastroenterology, Maria Hosp., SF-00180 Helsinki 18, Finland
Ann Clin Res; 13(3):154-155 1981

The association of the different types of polyps with gastric carcinoma and the development of carcinoma from benign polyps were investigated in 363 consecutive cases with endoscopically demonstrated polyp-like lesions. Discrimination between the different groups of adenomas, hyperplastic polyps and foveolar hyperplasia was often difficult; there were numerous transitional forms between the hyperplastic polyps and foveolar hyperplasia. These conditions might be different, morphologically related stages of the same process, which begins as simple hyperplasia of the glands. In some of the patients examined, hyperplastic polyps, polyps of the foveolar hyperplasia type, and inflammatory polyps disappeared spontaneously. It is probable that such polyps are caused by patchily disturbed cell kinetics of the foveolar epithelium: the renewal of such cells is more rapid than their destruction. The reversal of the disturbed cell kinetics should theoretically lead to the disappearance of such polyps. Gastric carcinoma was found in 27/363 cases (7.4%): in 38% of adenomas and 6.5% of hyperplastic polyps or foveolar hyperplasia. In 13 of the 27 cases, the gastric carcinomas were found in the gastric mucosa outside the polyps. It is suggested that the entire gastric mucosa should be considered diseased and possessing some malignant potential in the case of non-neoplastic polypoid lesions. (4 Refs)

18. FAMILY CHARACTERISTICS OF GASTRIC CARCINOMA.

Ihamaki T, Sipponen P
Div. Gastroenterology, Second Dept. Medicine, Univ. Helsinki, SF-00290 Helsinki 29, Finland
Ann Clin Res; 13(3):149-150 1981

Features of gastric carcinoma were investigated in 301 first-degree relatives of 73 consecutive probands with gastric carcinoma (series) and 358 relatives of 73 control probands computer matched from the general population by age and sex, residence and birth-place. In the series relatives, the prevalence of hyperplastic polyps and atrophic gastritis in the body and antrum, and the prevalence of intestinal metaplasia, epithelial atypia and achlorhydria were significantly higher than in the control relatives. These signs tended to occur at a younger age in the series, but statistical significance was found only for the occurrence of severe atrophic gastritis of the body, intestinal metaplasia, and epithelial atypia. In the relatives of the diffuse carcinoma patients the prevalences of atrophic gastritis of the body and antrum and intestinal metaplasia were significantly higher than in the controls. No such differences were found between the relatives of the intestinal carcinoma patients and their controls. Epithelial atypia and achlorhydria tended to appear at a younger age in the relatives of the diffuse carcinoma patients and the mean age of patients with epithelial dysplasia was significantly lower among the diffuse carcinoma relatives. (3 Refs)

19. FAMILY BEHAVIOUR OF GASTRIC CARCINOMA.

Lehtola J
Div. Gastroenterology, Univ. Central Hosp., SF-90220 Oulu 22, Finland
Ann Clin Res; 13(3):144-148 1981

The etiology of gastric carcinoma (GCA) was studied with particular attention to the different types in a statistical family study. There were 341 probands with histologically verified GCA diagnosed between 1962 and 1963; GCA was intestinal in 139 cases and diffuse in 67. In 2,243 relatives of the probands, the proportion with GCA was 3.53% if the proband had intestinal GCA, 4.99% if the proband had diffuse GCA, 2.12% if the proband had undifferentiated GCA, and 3.07 if the type of GCA in the proband was unknown. In 2,301 relatives of controls, these figures were, respectively, 2.9%, 1.17%, 3.39%, and 2.37%. The preceding figures were statistically significant only in relatives of probands with diffuse GCA. The relative risk of relatives of probands with diffuse GCA was 7.0 (p less than 0.005). An increased risk was seen only when the proband was female and the highest values were in the cases where the probands were young women. It is probable that genetic factors predispose the body to the influence of environmental factors in the development of GCA. (11 Refs)

20. GASTRITIS, ITS FATE AND SEQUELAE.

Siurala M
Div. Gastroenterology, Second Dept. Medicine, Univ. Helsinki, SF-00290 Helsinki 29, Finland
Ann Clin Res; 13(3):111-113 1981

A long-term follow-up study was conducted in the 1970's of morphologically verified gastritis in the body mucosa of 116 patients and was compared to the mucosa in 261 controls; both groups were initially seen between 1950 and 1970. Most subjects with originally normal mucosa developed superficial gastritis, while those with superficial gastritis often (50%) displayed atrophic changes at the end of follow-up. These findings indicate a general trend for progression of the gastritic changes with age, and that the progression to atrophic gastritis as a rule passed through the stage of superficial gastritis. Subjects with atrophic gastritis were characterized by a higher prevalence of gastric carcinoma, gastric polyps, intestinal metaplasia, and epithelial dysplasia, compared with controls. While these results do not definitively prove that atrophic gastritis is a precancerous lesion, they show that signs of a severe lesion of the body mucosa characteristic of type A gastritis commonly precede the diagnosis of an intestinal type of gastric carcinoma. (11 Refs)

INDUCTION OF GI CARCINOGENESIS IN ANIMALS

21. FURTHER STUDIES ON THE CARCINOGENESIS OF THE COLON OF THE RAT WITH SPECIAL REFERENCE TO THE ABSENCE OF INTESTINAL CONTENTS.

Rubio CA, Nylander G
Dept. Pathology, Karolinska sjukhuset, S-104 01 Stockholm, Sweden
Cancer; 48(4):951-953 1981

The proximal and distal ends of the ascending, transverse and descending colon of 67 Sprague-Dawley rats were severed and stitched to the abdominal wall. The remaining colon was anastomosed end to end. The disarticulated colon loop was rinsed 30x over 15 days to remove all traces of intestinal contents. The animals were then given sc injections of 1,2-dimethylhydrazine (21 mg/kg body wt) for 27 wk. During that period, the isolated loops were rinsed with saline once a wk. The rats were killed after 7 mo of treatment. Eighty-five tumors developed in the 67 animals: 20 in the isolated loops and 65 in the end-to-end anastomosed colon. The carcinogen employed reached the colonic loop through the circulation and induced (independently of bile acids) mucosal changes that led to the development of colonic tumors. (Author abstract) (15 Refs)

22. EXPERIMENTAL COLONIC CANCER IN A DOG.

Kamano T, Kurihara H, Kishino H, Mizukami K, Kidokoro T, Wakabayashi K, Kuwabara N
First Dept. Surgery, Juntendo Univ. Sch. Medicine, Tokyo 113, Japan
Jpn J Surg; 11(3):214-218 1981

The histogenesis, mode of proliferation, and metastatic spread of colonic neoplasm induced in a mongrel dog by anal application of N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG) were studied. ENNG suppositories were given continuously for 17 mo (a total of 15.8 g of ENNG was given). Bloody feces were first recorded after 6-mo treatment. After 17-mo treatment, a tumor appeared in the anal margin. The animal developed dyschezia, anorexia, and emaciation. Three mo after termination of ENNG treatment, the dog was sacrificed, and the tissues were subjected to histological examination. There was a thickening of the colonic wall, enlargement of the ileocecal, perigastric and tracheal bifurcation lymph nodes. Histologic examination of the colonic tumor showed undifferentiated carcinoma, squamous cell carcinoma, and malignant melanoma. Metastases to the regional and distant lymph nodes, lung, liver and renal glomeruli had the histology of undifferentiated carcinoma. Tumors detected in the stomach had the histology of well differentiated adenocarcinoma and signet ring cell carcinoma. (6 Refs)

MECHANISMS AND MODIFICATIONS OF GI CARCINOGENESIS

23. THE EFFECTS OF THE CARCINOGEN, 1,2-DIMETHYLHYDRAZINE, ON TURNOVER OF 3H-THYMIDINE LABELED CELLS FROM MUCOSAL GLANDS OF MOUSE COLON.

Richards TC
Dept. Anatomy, Sch. Medicine, Univ. Oregon, Health Sciences Center, Portland, OR, 97201
Anat Rec; 200(3):299-308 1981

The compound 1,2-dimethylhydrazine (DMH), administered weekly to mice for 20 wk induces tumors in the distal segment of colon. Tumors are preceded by enlargement of the mucosal glands resulting from increases in the number of total cells and 3H-thymidine labeled cells/crypt. Cells located in the crypt base normally undergo two-three divisions as they migrate toward the lumen, and they become post-mitotic in the upper crypt. It is not known if cells in these enlarged crypts have rates of turnover similar to cells in normal crypts. Groups of w/s female mice were treated with DMH (20 mg/kg body wt) for 3, 8, or 16 wk; controls were given 0.001 M EDTA. After treatment, the animals were injected with 3H-thymidine and killed 1 hr or 1, 2, 4, 7 or 17 days later. Autoradiographs were prepared from sections of distal colon. The total cells/crypt column in 30 crypts/animals were counted. Crypts were divided into 10 equal segments based on the crypt length and the labeled cells/segment were counted. The relative number of labeled cells and the distribution of these cells within crypts were similar in DMH-treated and control animals after 1 hr. However, as the cells migrated toward the lumen, the number of labeled cells doubled after 2 days and tripled after 4 days in DMH-treated animals but only doubled during the 4 days in controls. This difference was caused by retention of an increased number of dividing cells in the lower four segments of the crypts and suggests an increase in those cells that divide twice. In addition, increased numbers of labeled cells were retained in the upper three segments of DMH-treated animals after 4 days. These findings indicate that the crypt cells of DMH-treated animals are generally more immature than those of controls and this immaturity contributes to the enlargement of mucosal glands during carcinogenesis. (Author abstract) (22 Refs)

24. COLOSTOMY CLOSURE PROMOTES CELL PROLIFERATION AND DIMETHYLHYDRAZINE-INDUCED CARCINOGENESIS IN RAT DISTAL COLON.

Terpstra OT, Dahl EP, Williamson RC, Ross JS, Malt RA
(c/o Malt), Massachusetts General Hosp., Boston, MA, 02114
Gastroenterology; 81(3):475-480 1981

The influence of adaptive cell proliferation on colonic carcinogenesis was studied in male Fischer rats with a defunctioning transverse colostomy that was closed 4 wk later. Control observations were made in other rats after colonic transection, repeated at 4 wk, after laparotomy alone, or after permanent colostomy. Tumors were induced by 1,2-dimethylhydrazine (total dose, 300 mg/kg) over 11 wk, starting 2 days after the second operation. After creation of the colostomy, amounts of protein, RNA, and DNA in the distal colon halved in 4 wk (p less than 0.001), but returned to normal 7 days after restoration of colonic continuity. This reactive hyperplasia promoted the development of distal colonic carcinomas, as compared with rats having repeated transection of the bowel (incidence 32% vs 6%, p less than 0.03). Although the amounts of protein and nucleic acid in the proximal colon were unchanged by transverse colostomy, values increased by 18%-59% 4 wk after colostomy closure (p = 0.05-0.002); nonetheless, the yield of tumors in this segment was unaltered. Suture-line cancers were more common after repeat transection than after colostomy closure (76% vs 39%; p less than 0.01). These data confirm the promotional effect of increased cell proliferation on intestinal carcinogenesis. (Author abstract) (40 Refs)

BIOCHEMICAL, MORPHOLOGICAL AND IMMUNOLOGICAL ASPECTS OF GI CARCINOGENESIS

25. COMPARATIVE STUDY OF VILLOUS, VILLOTUBULAR, AND TUBULAR ADENOMAS IN THE COLON AND RECTUM.

Kozuka S, Nogaki M, Nogaki M, Ozeki T, Masumori S, Kitano H, Koshimura K
Dept. Pathology, Nagoya Univ. Sch. Medicine, Nagoya, Japan
Gan No Rinsho; 27(9):1118-1124 1981

Pathohistological examinations were performed in 712 patients with large intestine polyps, and the size of the lesion, the cancer occurrence rate, age and sex of the patients, etc were studied particularly in 410 patients with tubular adenomas, 115 with villotubular adenomas, and 43 with villous adenomas. The incidence of cancer was 9.0% in the tubular adenoma group, 26.1% in the villotubular adenoma group, and 25.6% in the villous adenoma group. The incidence of cancer among those with tumors that were either 2 cm in diameter or less or greater than 2 cm, respectively, was 7.6% and 48.1% in the tubular adenoma group, 22.8% and 50.0% in the villotubular adenoma group, and 7.4% and 47.6% in the villous adenoma group. Compared to tubular or villotubular adenomas of the same histological grade of malignancy, the villous adenomas were larger in av diameter and were observed more often in elderly patients. (24 Refs) (In JPN)

26. KINETICS OF THE NON-NEOPLASTIC MUCOSA OF THE LARGE BOWEL OF DIMETHYLHYDRAZINE-TREATED RATS.

Sunter JP, Watson AJ, Appleton DR
Dept. Pathology, Queen Elizabeth Hosp., Gateshead, Tyne and Wear, NE9 6SX, England
Br J Cancer; 44(1):35-44 1981

Administration of 1,2 dimethylhydrazine (DMH) to rats by weekly sc injections causes the development of multiple epithelial tumors of the large bowel. These appear to arise as localized dysplastic abnormalities in hitherto apparently morphologically normal crypts. This study was undertaken in order to examine cell proliferation in such apparently normal crypts of DMH-treated animals. A number of proliferative abnormalities are evident, including changes in the size of the crypts, changes in the disposition of proliferating cells within them and reduced cell-cycle times. The nature and the extent of the abnormalities vary from site to site along the length of the bowel, and reflect the vulnerability of the different segments of the bowel, not only to the carcinogenic effects of DMH, but also to short-term toxicity. (Author abstract) (23 Refs)

27. ELECTRON MICROSCOPY OF POLYPS OF THE COLON: I. COMPARATIVE STUDY OF THE EPITHELIAL CELLS OF ADENOMATOUS AND ADENOPAPILLARY POLYPS.

Balazs M
Dept. Pathology, Janos Hosp., Diosarok u. 1, H - 1125 Budapest, Hungary
Exp Pathol (Jena); 19(2):112-121 1981

By comparing the electron-microscopic pictures of adenomatous and adenopapillary polyps, the ultrastructural characteristics of premalignant epithelial dysplasia were studied. In highly differentiated adenomatous polyps, the ratio and the electron-microscopic appearance of absorptive and goblet cells did not differ from the epithelial cells of the normal mucosa of the colon. In the dysplastic regions of adenopapillary polyps, the intensive proliferation in several layers of undifferentiated epithelial cells, and the maturation disorder of absorptive and goblet cells, were observed. Severe changes occurred on the cell membrane as well as atypical vacuoles and dense bodies in the apical regions of the cell membrane. Several inclusion bodies of Leuchtenberger were observed, these being considered an important characteristic of malignant transformation. (Author abstract) (37 Refs)

28. ELECTRON MICROSCOPIC AND MICROSPECTROPHOTOMETRIC OBSERVATIONS IN SCIRRHOUS CARCINOMA OF THE STOMACH.

Iida F, Nagata T
Dept. Surgery, Kofu Municipal Hosp., 14-6, Saiwai-cho, Kofu 400, Japan
Jpn J Clin Oncol; 11(1):39-49 1981

An attempt was made to clarify the developmental behavior of scirrhous carcinoma (SC) through the use of electron microscopic and microspectrophotometric technics for estimating the DNA content of cancer cells in nine patients with SCs and five patients with well-differentiated adenocarcinomas (ACs). Electron microscopic observation of SCs revealed marked proliferation of collagen fibrils. Damaged cancer cells scattered along the collagen fibrils were prominent findings in the deep area of the lesion, but were rarely seen in the superficial and peripheral areas. In ACs, proliferation of collagen fibrils occurred to some extent, but not to the extent seen in SCs. The DNA distribution patterns in SCs, varied according to the area of the carcinoma. In the superficial and peripheral areas, the DNA content of the nuclei of cancer cell had a much wider range than that of normal tissues. Two peaks were found at the hyperdiploid and hypertetraploid ranges. The percentage of nuclei below the hyperdiploid range was higher in the deep area than in the other two areas in all nine cases. In the ACs, the histogram showed varying distributions of one to two peaks. Differences in the DNA distribution pattern according to area were not discernible. The percentages of nuclei below the hyperdiploid range were found to be almost identical among the three areas. The results suggested that the scirrhous area of the carcinoma has little significance for tumor growth and that growth can be determined from the scattered cancer cells in the edematous stroma at the periphery of the lesion. (11 Refs)

29. GASTRO INTESTINAL LYMPHOMAS: A RETROSPECTIVE ANALYSIS.

Saksena A, Shankur R, Rajvanshi VS
Dept. Pathology, G. S. V. M. Medical Coll., Kanpur, India
Indian J Cancer; 18(2):123-127 1981

Between 1969 and 1979, 48 lymphomas of the gastrointestinal (GI) tract were identified out of 426 cases of lymphomas. Most of the 48 GI lymphomas were of the non-Hodgkin's group (79.17%) with 20.83% in the Hodgkin's disease group. Approx half of the cases were restricted to the second and third decades; only 12.5% presented after 50 yr. All age groups showed a male preponderance. Most patients presented with signs of intestinal obstruction, progressively increasing abdominal lump, and loose motions. Wt loss and anorexia were common. The primary sites were the ileum (35.4%), colon (20.8%) and only one case (2.08%) occurred in the duodenum. Grossly, approx 60% showed a diffuse infiltration of the intestinal wall with flat, greyish-white, plaque-like lesions and concomitant loss of mucosal pattern. The draining mesenteric lymph nodes were enlarged in 75%. Follicular hyperplasia with a sinus reaction of lymph nodes was found in half of the cases, and the specific lesion in the other half. Hodgkin's disease was the mixed cellularity type, while the non-Hodgkin's lymphomas were lymphocytic lymphoma, poorly differentiated type (33.3%) and lymphocytic lymphoma, intermediate differentiation (22.9%). The clinicopathologic findings and their relation to possible etiological factors were discussed. (17 Refs)

PANCREATIC CARCINOGENESIS

30. PANCREATIC CANCER.

Cohn I, Hastings PR
Dept. Surgery, Louisiana State Univ., 1542 Tulane Ave., New Orleans, LA, 70112
UICC Tech Rep Ser. Vol. 57, Issue 12, 142 pp., 1981.

The objectives of the International Union Against Cancer Workshop were to bring together a small group of active workers in the basic aspects of pancreatic cancer (PC) with the hope that by their carefully planned interchange, they might summarize current information and provide some guidelines for future research. Topics discussed included the epidemiology of PC (international incidence data, time trends, urban/rural differences, socioeconomic differences, and risk factors), pathology of PC (nonendocrine: types of PC), cell structure and function of endocrine PC (synopsis of current views on pancreatic islet cytology, analysis of cell structure and secretory products in endocrine PCs, experimental tumors, mixed endocrine-exocrine PC, and perspectives for future work), carcinogenesis (pancreatic carcinogenes, carcinogen metabolism, and histogenesis of PC), animal models, biology of pancreatic tumor cells, tumor markers (carcinoembryonic antigen (CEA), pancreatic oncofetal antigens (POA), comparison of POA and CEA, search for other new PC markers, comparison of CEA and anti-CEA reactive substances in colonic and pancreatic tumors, identification and evaluation of protein degradation products resulting from protease activities associated with PC, leukocyte adherence inhibition, galactosyl transferase isoenzyme in PC, and radioimmunodetection), effects of diet on the exocrine pancreas, aims and decision in PC with regard to the relationship between tumor and host (current methods of treatment, prognostic factors, and therapeutic strategy), and conclusions and recommendations for future work. (432 Refs)

31. CHANGES OF AMYLASE DURING EXPERIMENTAL PANCREATIC CARCINOGENESIS IN HAMSTERS.

Takahashi M, Nagase S, Takahashi M, Kokubo T, Hayashi Y
Dept. Chemistry, Sasaki Inst., Kanda Surugadai 2-2, Chiyoda-ku, Tokyo 101, Japan
Gan; 72(4):615-619 1981

Changes of amylase activity and isozymic pattern in the serum, urine, ascites, pancreas and parotid gland of hamsters during pancreatic carcinogenesis induced by N-nitrosobis(2-oxopropyl)amine (BOP) were examined. During the early stage of pancreatic carcinogenesis, amylase activity in the urine was greatly increased and the pancreatic type of isozyme increased in the serum and urine, but in the terminal stage, the activity decreased and the isozymic pattern reverted to normal. These alterations of amylase could be due to focal pancreatitis around dysplastic ductules and small carcinoma lesions causing leakage of pancreatic juice. This phenomenon may be of value in diagnosis of the early stage of pancreatic cancer. (Author abstract) (8 Refs)

REVIEWS AND OTHER RELATED STUDIES

32. COLON POLYPS: WHEN ARE THEY MALIGNANT?

Posner GL, Sharma DS
Div. Gastroenterology, Jewish Hosp. and Medical Center of Brooklyn, 555 Prospect Place, Brooklyn, NY, 11238
Geriatrics; 36(8):57-60 1981

A clinical review is made of diagnostic approach, etiology, size and shape, and treatment for polyps of the colon and rectum. The different histologic entities include non-neoplastic (inflammatory, infectious, and hyperplastic), neoplastic (adenoma, carcinoma and sarcoma, metastatic, and others), and miscellaneous (polyposis cystica profunda, pneumatosis cystoides, intestinalis, Cronkhite-Canada syndrome, hamartoma, and juvenile polyp). Diagnosis should involve history and physical examination, and, as indicated, stool studies, flexible fiberoptic sigmoidoscopy, air-contrast barium enema, and colonoscopy. Etiology of polyps is not known, but the various syndromes can be summarized. Those involving high risk of malignancy are familial polyposis, Gardner's syndrome, disseminated gastrointestinal polyposis, and Turcot's syndrome. Low risk diseases are Peutz-Jeghers syndrome, juvenile polyposis and variants, and multiple adenomas. Cronkhite-Canada syndrome and Cowden's disease present no known risk. Polyps less than 5 mm are not usually cancerous, but should be removed or watched closely after biopsy. Those greater than 2 cm are much more dangerous: the incidence of malignancy is in the range of 10-50%. The majority of polyps can be removed by snare cautery at the same time of colonoscopy, even in very sick patients. The two most common complications are perforation (0.22%) and hemorrhage (1.9% with polypectomy). (11 Refs)

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NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. THE GENETIC TOXICOLOGY OF ALDRIN AND DIELDRIN.
   Ashwood-Smith MJ
   Environmental Toxicology Res. Group, Dept. Biology, Univ. Victoria, Victoria, BC V8W 2Y2, Canada
   Mutat Res; 86(2):137-154 1981

RADIATION CARCINOGENESIS

2. EFFECTS OF LOW-LEVEL RADIATION ON BIOLOGIC SYSTEMS: A LITERATURE REVIEW.
   Best TL, Hoditschek B
   Eastern New Mexico Univ., Portales, NM
   Effects of Low-Level Radiation on Biologic Systems: A Literature Review. Available from National Technical Information Service, Springfield, VA, as SAND-80-7143:, 246 pp., 1981.
3. PHOTOCARCINOGENESIS: AN OVERVIEW.
   Forbes PD
   Skin and Cancer Hosp., 3322 North Broad St., Philadelphia, PA, 19140
   J Invest Dermatol; 77(1):139-143 1981

DIETARY FACTORS IN CARCINOGENESIS

4. EPIDEMIOLOGICAL CORRELATIONS BETWEEN DIET AND CANCER FREQUENCY.
   Correa P
   Louisiana State Univ. Medical Center, New Orleans, LA, 70112
   Cancer Res; 41(9,part2):3685-3689 1981
5. ROLE OF DIETARY FIBER IN DIVERTICULAR DISEASE AND COLON CANCER.
   Talbot JM
   Life Sciences Res. Office, Federation of American Societies for Experimental Biology, Bethesda, MD, 20014
   Fed Proc; 40(9):2337-2342 1981

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

6. PRIMARY HEPATIC CANCER IN ALCOHOLICS.
   Tamburro CH, Lee HM
   Liver Res. Center, Div. Digestive Diseases and Nutrition, Univ. Louisville Health Sciences Center, 511 South Floyd St., Louisville, KY, 40232
   Clin Gastroenterol; 10(2):457-477 1981
7. PANCREATIC CANCER AND ALCOHOL.
   Okuda K, Ohnishi K
   Dept. Medicine, Chiba Univ. Sch. Medicine, 1-8-1 Inohana, Chiba City (280), Japan
   Clin Gastroenterol; 10(2):479-484 1981
8. HELMINTHS IN THE INDUCTION OF CANCER. II. SCHISTOSOMA HAEMATOBIUM AND BLADDER CANCER.
   Schwartz DA
   Inst. Medicine, Far Eastern Univ., Manila, Philippines
   Trop Geogr Med; 33(1):1-7 1981
9. GENETICS OF WILMS'S TUMOR.
   Matsunaga E
   Dept. Human Genetics, Natl. Inst. Genetics, Mishima, Shizuoka-Ken, 411, Japan
   Hum Genet; 57(3):231-246 1981

CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

10. NEOPLASMS: COMPARATIVE PATHOLOGY OF GROWTH IN ANIMALS, PLANTS, AND MAN.
    Kaiser HE
    Dept. Pathology, Univ. Maryland Sch. Medicine, Baltimore, MD
    Neoplasms: Comparative Pathology of Growth in Animals, Plants, and Man. Baltimore, Williams and Wilkins, 908 pp., 1981.
11. PULMONARY CARCINOGENESIS: ARYL HYDROCARBON HYDROXYLASE.
    McLemore TL, Martin RR
    Dept. Medicine, Baylor Coll. Medicine, Houston, TX, 77030
    Cancer Treat Res; 1:1-34 1981
12. THE GENETIC TOXICITY OF HYDROXYLAMINES.
    Marfey P, Robinson E
    Dept. Biological Sciences, State Univ. New York at Albany, Albany, NY, 12222
    Mutat Res; 86(2):155-191 1981

MODIFICATION OF CARCINOGENESIS

13. MODIFYING FACTORS OF CHEMICAL CARCINOGENESIS.
    Beliaev II, Litvinov IuA
    Medical Inst., Gorki, USSR
    Gig Sanit; (6):59-62 1981
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14. ANTIPROLIFERATIVE EFFECTS OF RETINOIDS RELATED TO THE CELL CYCLE-SPECIFIC INHIBITION OF ORNITHINE DECARBOXYLASE.
    Russell DH, Haddox MK
    Dept. Pharmacology, Univ. Arizona Coll. Medicine, Tucson, AZ, 85724
    Ann NY Acad Sci; 359:281-297 1981

VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

15. PATHOGENESIS OF THYMIC LYMPHOMAS IN C57BL MICE.
    Boniver J
    Laboratoire d'Anatomie Pathologique, Tour de Pathologie B. 23, Universite de Liege au Sart Tilman, 4000 Liege, Belgium
    Pathol Res Pract; 171(2):268-278 1981

METHODOLOGY IN CARCINOGENESIS RESEARCH

16. CRITICAL ASSESSMENT OF THE VALUE OF IN VITRO CELL TRANSFORMATION FOR PREDICTING IN VIVO CARCINOGENICITY OF CHEMICALS.
    Brookes P
    (c/o Lohman, P. H.), Medical Biological Lab. TNO, P.O. Box 45, 2280 AA Rijswijk, The Netherlands
    Mutat Res; 86(2):233-242 1981

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17. MAMMALIAN GENETICS AND CANCER.
    Russell ES
    Jackson Lab., Bar Harbor, ME, 04609
    Prog Clin Biol Res 45: 327 pp., 1981.

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Gastrointestinal Tract and Pancreas

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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PREVALENCE OF GI CANCER IN HUMAN POPULATIONS

1. EPIDEMIOLOGY OF GASTROINTESTINAL CANCER.

Miller AB
NCIC Epidemiology Unit, Univ. Toronto, McMurrich Building, Toronto, Ontario M5S 1A8, Canada
Compr Ther; 7(8):53-58 1981

An epidemiological study is presented which attempts to quantify the problems and obtain clues as to the cause of gastrointestinal (GI) cancers in North America and elsewhere. Cumulative incidence to age 75 for various cancers of the GI tract as determined by the Third National Cancer Surve y is presented. The range of incidence throughout the world of esophageal and liver cancer is greatest, followed by gallbladder, colon, stomach, rectal, and pancreatic cancer. The sex ratios are similar in incidence for colon cancer, moderately excessive for males with stomach, rectum, and pancreatic cancers, and substantially excessive for males with esophageal and liver cancers. An excess in females occurs with gallbladder cancer. Similarities in the frequency of occurrence for different diseases suggest common causes: the causes of esophageal cancer in men and women are probably different, while those for colon, rectal, and pancreatic cancers in both sexes may be similar, as are those for liver and esophageal cancer in men and for breast, endometrial, and ovarian cancer in women. The inverse correlation of colon cancer with stomach cancer suggests that entirely different causes may be involved. The epidemiologic knowledge of esophageal, stomach, colon and rectal, gallbladder, liver, and pancreatic cancers is reviewed. It appears that protective factors for one cancer are different from factors that appear to be carcinogenic for others. Future studies will identify interactions among factors and will specify which are responsible in different areas. (15 Refs)

2. MORBIDITY FROM CANCER IN LA PAZ, BOLIVIA.

Rios-Dalenz J, Correa P, Haenszel W
Casilla 490, La Paz, Bolivia
Int J Cancer; 28(3):307-314 1981

Data from a population-based Cancer Registry in La Paz, Bolivia, are presented. The city is located at approx 4,000 meters above sea level and has a strong cultural influence consisting of Aymara Indians immigrating from the altiplano. Incidence rates in females are high for cancer of the cervix, the gallbladder and the thyroid gland. Males display unusually high rates of testicular cancer. Stomach cancer rates are lower than among other Andean populations. Smoking-related cancer and cancers related to sex-hormones are lower than av in incidence. Cancer of the nasal mucosa and paranasal sinuses is unusually high in frequency. (Author abstract) (20 Refs)

3. EPIDEMIOLOGY OF GASTRIC CANCER IN CHILE.

Armijo R, Detels R, Coulson AH, Medina E, Orellana M, Gonzalez A
Div. of Epidemiology School of Public Health, Univ. of California, Los Angeles, CA, 90024
Rev Med Chil; 109(6):551-556 1981

Japan has the highest gastric cancer mortality (GCM), followed closely by Chile and Costa Rica. The GCM in Chile was studied in 1957-1975 period. The extreme south and north had the lowest values for GCM were 20/100,000, which increases as approaching the center. The highest values for GCM were 50/100,000, found in 3 agricultural provinces 200 kilometers south of Santiago. The GCM decreased slightly worldwide between 1957 and 1972, this is true for Chile, except for the high risk areas. Chile has vast reserves of natural nitrates and they are used widely as fertilizers. Gastric cancer patients in controlled, matched studies were shown to have been residents longer in the areas of high nitrates utilization. Nitrates and nitrites were measured in saliva and urine of urban children, and edible vegetables of different areas, but no significant differences could be found. All factors, which could influence the results are analyzed and discussed. (10 Refs) (In SPA)

4. THE MALIGNANT DIGESTIVE TUBE TUMORS IN THE POPULATION OF URUGUAY. PART THREE - THE MALIGNANT INTESTINAL (RECTUM EXCLUDED) AND RECTAL TUMORS.

Carro Tunessi M, Fernandez Giuliani J, Gianelli Ferrero S, Ketzoian Aparikian C, Rovigo Guanco A, Vidal Gaggiano L, Werner Cowalesky MA

Departamento y Catedra de Higiene y Medicina Preventiva, Facultad de Medicina del Uruguay, Montevideo, Uruguay

An Fac Med Univ Montev; 4(1):35-40 1981

The data for the survey were obtained from the death certificates for the census yr 1963 and 1975, they were separated according to the sex and the location of the tumors. These results were compared with the data from the international survey for 1975. The malignant intestinal (rectum excluded) tumor data were similar for both yr and both sexes, the females predominated in both yr. There was a decrease in the mortality of rectal cancer in yr 1975 compared to the yr 1063, which was verified for both sexes and in almost all the age groups, but males predominated in both yr. The rectal cancer mortality for males started in 15-24 yr age group and females in 25-34 yr age group. Compared with the international survey the intestinal (rectum excluded) cancer, there was an increase for the males in both surveys, for the females the international survey demonstrated a decrease, but in Uruguay for the yr 1975 the data were the same or increasing. For the rectal cancer both surveys for the yr 1975 showed a decrease. (5 Refs) (In SPA)

5. THE MALIGNANT DIGESTIVE TRACT TUMORS IN THE POPULATION OF URUGUAY.

Carro Tunessi M, Fernandez Giuliani J, Gianelli Ferrero S, Ketzoian Aparikian C, Rovigo Guanco A, Vidal Gaggiano L, Werner Covalesky A

Catedra de Higiene Medicina Preventiva, Facultad de Medicina de Uruguay, Montevideo, Uruguay

An Fac Med Univ Montev; 4(1):21-26 1981

This survey was based on the examination of the death certificates. There were no previous surveys of the Uruguay population mortality due to the malignant digestive tract tumors, their location and sex. The digestive tract was divided according to the Committee of Experts of the World Health Organization to: esophagus, stomach, intestines and rectum. This survey was taken in 1963 and in 1975. The data obtained in 1975 were compared with the international data. There was no difference in the total mortality or the distribution by sex between the two yr, but there were differences in location: the mortality of the stomach cancer decreased and the mortality of the intestinal cancer increased. When comparing international and Uruguay data, there was an inversion in the stomach and rectum cancers. In Uruguay the stomach cancer was third and the rectum cancer was fourth, the opposite was true in the international survey. (3 Refs) (In SPA)

6. MORTALITY FROM CANCER OF THE DIGESTIVE SYSTEM IN ITALY: 1950-1975 CROSS-SECTIONAL RATES AND COHORT ANALYSIS.

Mastrandrea V. La Rosa F, Cresci A, Pannelli F
(c/o La Rosa) Inst. Hygiene, Camerino Univ., 62032 Camerino, Italy
Am J Epidemiol; 114(2):218-228 1981

In this study of mortality from cancer of the digestive system in Italy, 1950-1975, both cross-sectional rates and cohort analysis were used. The study found that in both sexes age-standardized rates for cancer of the colon, rectum, liver and biliary tract, and pancreas are increasing whereas the rates for cancer of the stomach are decreasing. Rates for esophagus cancer have remained fairly constant. Cohort analysis showed different trends for selected sites. As to cancer of the stomach, for both sexes, cohorts born up until about 1881 have constant or increasing rates; cohorts born after 1881 have declining rates. For cancer of the esophagus in males the rates reach a peak in the 1896 birth-cohort; cohorts born prior to 1896 show an increase in rates and cohorts born later show a decline. For cancer of the colon, liver and biliary tract, and pancreas, the rates rise constantly for all ages and all cohorts in both sexes. The rates for cancer of the rectum rise after age 75 whereas below that age the rates tend to level off and decline. (Author abstract) (40 Refs)

7. EPIDEMIOLOGICAL ASPECTS OF ESOPHAGEAL CANCER.

Ruggieri M, Tosato F, De Rocco K, Lepore M, Cipriano E, Paolini A
IV Cattedra di Clinica Chirurgica Generale e Terapia Chirurgica, Universita degli Studi di Roma, Rome, Italy
Recenti Prog Med; 70(5):545-556 1981

The epidemiology of esophageal cancer (EC) is reviewed and epidemiological data are presented for a series of patients subjected to surgery for EC at a clinic during the period 1971-1980. The factors probably favorable for the development of EC are ethyl alcohol, tobacco, polycyclic aromatic hydrocarbons (benzopyrene, dibenzanthracene, and 3-methylcholanthrene) present in smoked foods, nitrosamines, molybdenum, tannin, hot food, diet deficient especially in thiamine, riboflavine, and vitamin C, esophageal stenosis, peptic reflux esophagitis, brachyesophagus, achalasia of the cardia, gastric resection, and Plummer-Vinson syndrome. The epidemiological analysis of the patients treated during the 1971-1980 period showed that all patients were in the age bracket 42-75 with a mean of 59.3 yr, and that women accounted for 5.2% of the patients only. Alcohol consumption (1 liter/day) was established in 18.5% of the patients, alcohol consumption and smoking (10 or more cigarettes/day) in 52.5%, smoking only in 18.5%, and neither smoking nor alcohol consumption in 10.5%. The cervical third of the esophagus was affected in 10.5% of all cases, the thoracic third in 34%, and the abdominal third in 55.5%. (28 Refs) (In ITA)

8. EPIDEMIOLOGY OF CANCER.

Pawlega J
Pracownia Epidemiologii, Oddzial Instytutu Onkologii w Krakowie, ul. Garncarska 11, 31-115 Krakow, Poland
Przegl Lek; 38(5):447-451 1981

Cancer epidemiological data are presented for Krakow (urban area) and a nearby rural area for the period from 1965 on the basis of Cancer Registry data. The overall standardized cancer morbidity (per 100,000 population) in men in Krakow was 285 (70.9 for lung cancer, 35.1 for gastric cancer, 22.9 for skin cancer, 12.3 for pancreatic cancer, and 11.0% for urinary bladder cancer). The overall cancer mortality for men in the rural area was 177.1 (38.9 for lung cancer, 33.1 for gastric cancer, 9.6 for skin cancer, 8.3 for prostate cancer, and 8.0 for urinary bladder cancer). The cancer morbidity for women in Krakow was 201.1 (37.7 for breast cancer, 22.0 for cancer of the uterine cervix, 14.8 for gastric cancer, 14.9 for skin cancer, and 12.7 for lung cancer). The corresponding figures for the rural women were 122.1 (overall morbidity); 17.2 for gastric cancer, 17.8 for breast cancer. The percentage of cases diagnosed histologically was higher among the urban than among the rural patients, and the percentage of the patients not receiving antitumor therapy was higher among the latter. The relative 5-yr survival rates in men were higher among the urban patients than among the rural ones for all major localizations (lips, stomach, rectum, larynx, lungs, prostate, and bladder) except skin cancer, and the relative 5-yr survival of the urban women was higher for all major localizations (cancer of the stomach, skin, breasts, uterine cervix, endometrium, ovaries, and leukemia). (16 Refs) (In POL)

9. ESOPHAGEAL CANCER RESEARCH IN THE PEOPLE'S REPUBLIC OF CHINA.

Wu HH
Dept. Radiation Oncology, Cancer Res. Inst., Chinese Acad. Medical Sciences, Peking, People's Republic of China
Ann Otol Rhinol Laryngol; 90(4,part1):359-363 1981

Esophageal cancer, which accounts for 21% of all cancer deaths in China, has been the subject of epidemiology studies in the three areas of the country where the disease is most prevalent. In the area of the highest mortality rate, the first field research unit was established to study cancer in high-risk areas. The investigations of this unit for the last 20 yr are discussed, including the design and implementation of the studies. The geographic, dietary and cultural factors in the etiology of esophageal cancer are examined. The results of the studies and the clinical applications are explored. (Author abstract) (no Refs)

10. THE GASTRIC CANCER IN CHIRIQUI - FREQUENCY AND SOME EPIDEMIOLOGIC DATA.

Arosema A L
Panama
Rev Med Caja Seguro Soc; 13(1):160-165 1981

Panama is situated between Colombia and Costa Rica both countries with high incidence of gastric cancer. Panama's province of Chiriqui (C) is bordering on Costa Rica. The gastric cancer rate for C was 3.49/100000, this was the av for the three yr studied (1975-1977). The reported values for Costa Rica were 34/100000 for women and 64/100000 for men, which are similar to those found in Chile and not too far behind Japan with the highest values in the world. The frequency and the epidemiologic data for C coincide with other countries except for the blood group, which was predominantly O. Matson and Swamson reported that A and B blood groups probably belonged to European descendents and the O blood was predominant in the American native population, which constitute the majority in the C province. The areas of high frequency of gastric cancer in Colombia and Costa Rica are mostly settled by European descendents. The low frequency of gastric cancer in C when compared with high values found in neighboring Costa Rica are unexpected. The environmental factors, which are suspected to influence the high rate of gastric cancer, are found in C like: high mineral content of some areas especially copper, the volcanic zone and high consumption of smoked meats. The suspected protective environmental factors are also present: low altitude, adequate consumption of milk, fresh fruit and vegetables, better conservation of food by refrigeration and the predominant O blood group of the native population. (10 Refs) (In SPA)

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN GI CARCINOGENESIS

11. ASBESTOS, AN ENVIRONMENTAL POLLUTANT.

Zamfir G, Diaconu R
Institutul de igiena si sanatate publica, Iasi, Romania
Igiena; 30(1):1-9 1981

Studies on the carcinogenic effect of asbestos are reviewed. One hundred and eighty-nine cases of cancer were found among 623 workers exposed to asbestos for more than 20 yr in New York and New Jersey against an expected mortality of 47.2. Lung cancer was found in 84 cases, pleural mesothelioma in 8, peritoneal mesothelioma in 24, cancer of the stomach, colon, rectum, and esophagus in 41, and cancer of other localizations in 32. Positive correlation was found between digestive tract cancer mortality and the product of exposure. There is no conclusive evidence of increased incidence of pleural and peritoneal mesothelioma due to ingestion of drinking-water containing asbestos. (39 Refs) (In RUM)

12. ASBESTOSIS AND PUBLIC HEALTH.

Liddell FD
Dept. Epidemiology and Health, McGill Univ., 3775 University St., Montreal, PQ H 3A 2B4, Canada
Can Med Assoc J; 125(3):237-239 1981

Asbestos (AB) and AB-related disease are discussed. The most hazardous AB seem to be crocidolite and the least, chrysotile. Exposure-response relationships, which for lung cancer appear to be linear, are considered. The fiber gradient, which is steeper for mesothelioma than other responses, is discussed. The association between AB and gastrointestinal and laryngeal cancer is considered. Diagnosis of asbestosis is far from standard since no clinical signs are specific and some history of AB exposure is required. It has been shown that among AB workers, cigarette smoking increases the risks of lung and laryngeal cancer but not mesothelioma or gastrointestinal cancer and perhaps not asbestosis. In all AB-related diseases there is a long interval between the first exposure and the onset of symptoms. Safety limits for occupational AB exposure are discussed. Nonoccupational AB exposure is considered. The possible of use of AB substitutes and implications of their use are discussed. No asbestos control limit can guarantee absolute safety. (27 Refs)

13. CANCER RISK IN PESTICIDE-EXPOSED AGRICULTURAL WORKERS.

Barthel E
Bezirksfachkrankenhaus fur Lungenkrankheiten und Tuberkulose, Amsee 1, DDR-2060 Waren (Muritz), E. Germany
Arch Geschwulstforsch; 51(7):579-585 1981

Cancer risk was studied in 1,658 agricultural workers who had been exposed to pesticides for at least 5 yr in a cohort study. Malignant tumors were found in 169/1,658 cases; the tumors were confirmed histologically in 124/169 cases. Tumors of the esophagus, nasal cavity, soft tissues, lymphoid tissue, skin melanoma, lymphosarcoma, and lymphocytic leukemia were diagnosed in 1 case each. Other tumors included stomach in 21 cases, rectum in 7, liver in 2, gallbladder in 2, pancreas in 7, larynx in 4, trachea, bronchi, and lungs in 59, skin in 19, prostate in 11, penis in 2, urinary bladder in 7, brain in 2, and thyroid gland in 2. Lymphogranulomatosis was diagnosed in two cases, plasmocytoma in three, and myeloid leukemia in two. The difference between the exposed group and general epidemiological data was significant for lung cancer only (50 cases among exposed patients from 1970-1978 versus an expected value of 27.5). The av length of exposure of the lung cancer patients was 13.6 yr (6-23 yr), and the av latent period was 17.5 yr (6-29 yr). The higher incidence was not related to smoking habits, which suggests the etiological role of pesticide exposure. Based on intraindividual exposure data, experimental data, and on the use of pesticides in East Germany, the pesticides of greatest concern are arsenic-containing compounds, dicophane (DDT), lindane, and phenoxy acids. (21 Refs) (In GER)

14. AN EPIDEMIOLOGICAL SURVEY OF EIGHT OIL REFINERIES IN BRITAIN.

Rushton L, Alderson MR
Div. Epidemiology, Inst. Cancer Res., Sutton, Surrey SM2 5PX, England
Br J Ind Med; 38(3):225-234 1981

A mortality study of workers employed for at least 1 yr between 1 January 1950 and 31 December 1975 at eight oil refineries in Britain has been carried out. Over 99% of the population were successfully traced to determine their vital status at 31 December 1975. The mortality observed in the study population was compared with that which would be expected from the mortality rates for the all male population of England and Wales, and Scotland, with adjustment for regional variation in mortality for the English and Welsh refineries. The overall mortality observed was considerably lower than that expected on this basis, as was the mortality from heart disease, stroke, bronchitis, and pneumonia. The observed number of deaths from all neoplasms was also very much less than expected, a result almost entirely due to a large deficit of observed deaths from lung cancer. Raised mortality patterns were found in several refineries for cancers of the esophagus, stomach, intestines, and rectum, although no location was consistently high for all these causes of death. Different yr-of-entry cohorts and job groups were also affected. In general, mortality from these causes increased as length of service and interval from starting work increased. There were also significantly more observed deaths than expected from cancer of the nasal cavities and sinus, and melanoma. Further work is required to ascertain whether these are due to an occupational factor and, if so, to identify the physical or chemical nature of the risk. (Author abstract) (32 Refs)

15. MORTALITY OF UNITED KINGDOM ACRYLONITRILE POLYMERISATION WORKERS.

Werner JB, Carter JT
Health and Safety Executive, London W2 4TF, England
Br J Ind Med; 38(3):247-253 1981

The mortality of 1,111 men who worked on the polymerization of acrylonitrile and the spinning of acrylic fiber from 1950 to 1968 was surveyed up to the end of 1978. Seventy-nine deaths were identified. The population was drawn from six factories, where polymerization started before 1968, in England, Wales, Scotland, and Northern Ireland. In the group of men exposed to acrylonitrile for at least 1 yr the total number of deaths was smaller than expected. An excess of deaths from all cancers was found, arising mainly from cancers of the lung, stomach, colon, and brain, but the excess was not statistically significant. Significant excesses of stomach cancer overall and in those aged 55-64, and of lung cancer in those aged 15-44 were found. Consideration of deaths according to factory indicated that the excesses of stomach cancer may have been due to regional factors. The excess of lung cancer was investigated further in view of the fact that, unusually, it occurred in relatively young men, but no consistent difference between the duration of exposure to acrylonitrile of the three young patients with lung cancer and matched controls was found. The study is limited and further analysis in the future is needed. The results are not conclusive and neither add to nor detract from existing suspicions that acrylonitrile is a human carcinogen but, taken together with evidence from other studies, indicate the necessity for the continuing surveillance of the exposed population in the United Kingdom. (Author abstract) (9 Refs)

DIETARY AND DIGESTIVE FACTORS IN GI CARCINOGENESIS

16. COMPARISON OF THE MUTAGENICITY OF THE DIET IN RELATION TO MORTALITY FROM GASTRIC CANCER. II. MUTAGENICITY OF THE FOODS INGESTED BY THE INHABITANTS OF THE COUNTRYSIDE OF NARA AND KAGOSHIMA (MEETING ABSTRACT).

Michioka I, Kamiyama S
Dept. Hygiene, Akita Univ., Sch. Medicine, Hondo, Akita 010, Japan
Nippon Eiseigaku Zasshi; 36(1):178 1981

Foods to be consumed by the inhabitants of the villages in Haibara-machi, Nara Prefecture, and Togo-cho, Kagoshima Prefecture, which have different mortalities from gastric cancer, were frozen and air-mailed to this facility where they were thawed and the mutagenicity of the acetone-soluble fraction of the ether:petroleum ether (1:1) extract of the homogenate of the edible part was determined by the Ames' method with Salmonella typhimurium TA100. The foods with a relative mutagenicity rate of less than 1.5, 1.5-3.0 and more than 3.0 in the extract were designated negative, false-positive and positive, respectively. The rate of ingestion of negative and positive foods was strongly related to the mutagenicity of the foods for Akita and Iwate. However, in Nara the positive mutagenicity rate was low compared to that of gastric cancer mortality, which was high. The presence of some factors which promote the action of the mutagenic substances in foods on the gastric epithelium was thought to be responsible for the incidence of gastric cancer in Nara. (no Refs) (In JPN)

17. GASTRIC JUICE N-NITROSAMINES IN HEALTH AND GASTRODUODENAL DISEASE.

Reed PI, Haines K, Smith PL, House FR, Walters CL
Gastrointestinal Unit, Wexham Park Hosp., Slough, Berkshire SL2 4HL, England
Lancet; 2(8246):550-552 1981

The concentrations of total extractable N-nitroso compounds, pH, and nitrite levels were measured in fasting gastric juice, which was also cultured for bacteria, from 50 healthy volunteers and 217 patients with common upper gastrointestinal complaints. The concentrations of N-nitroso compounds and pH levels rose significantly with age. Sex and cigarette smoking had no significant effect. There was a positive correlation between pH and N-nitroso concentration, and between pH and an increase in the concentration of nitrites. A significant relation was demonstrated between raised N-nitroso and nitrite levels and growth of nitrate reductase-positive microorganisms. These results demonstrate for the first time in man the interrelations of N-nitrosamine concentration, pH, gastric juice nitrite, and nitrate-reducing bacteria. The findings are considered in relation to the risks of development of gastric cancer in man. (Author abstract) (30 Refs)

18. COMPARISON OF THE MUTAGENICITY OF THE DIET IN RELATION TO MORTALITY FROM GASTRIC CANCER. I. THE FOODS EATEN IN NARA AND KAGOSHIMA FROM THE VIEWPOINT OF THE MUTAGENICITY OF THE FOODS EATEN IN AKITA AND IWATE (MEETING ABSTRACT).

Kamiyama S, Michioka I
Dept. Hygiene, Akita Univ., Sch. Medicine, Hondo, Akita 010, Japan
Nippon Eiseigaku Zasshi; 36(1):177 1981

The mutagenicity of the foods of the inhabitants of the farm and mountain villages of Nara and Kagoshima which have contrasting mortality from gastric cancer was examined and compared with that of the inhabitants of Akita and Iwate, reported earlier. The diet of the head or housewife of the family of 30 and 31 households, respectively, in Haibara-machi, Nara Prefecture, and Togo-cho, Kagoshima Prefecture, selected randomly in May 1980 was recorded for 2 days. The foods which were eaten significantly more in a mutagenic diet and those which were eaten significantly more in a nonmutagenic diet were referred to as positive and negative foods, respectively. The percentage of positive foods eaten in Nara and Kagoshima was similar to that in Akita and Iwate, respectively. On the other hand, the percentage of negative foods was the highest in Kagoshima, followed in order by Nara, Iwate and Akita. The number of negative foods was plotted against that of the positive foods to obtain a stochastic ellipse. There was a clear difference between the number of positive and negative foods in a positive diet and that in a negative diet. The mortality for gastric cancer between 1973 and 1977 was 68.05, 38.56, 27.27 and 11.03 per 100,000 for Nara, Akita, Iwate and Kagoshima, respectively. The number of the negative and positive foods consumed was clearly reflected in these mortalities. (no Refs) (In JPN)

19. DETECTION OF NITROSAMINES IN A COMMONLY USED CHEWING TOBACCO.

Bhide SV, Pratap AI, Shivapurkar NM, Sipahimalani AT, Chadha MS
Cancer Res. Inst., Bombay 400 012, India
Food Cosmet Toxicol; 19(4):481-483 1981

Ethanol and acetone-water extracts were made from Pandharpuri, a brand of chewing tobacco popular in India. The extracts were analyzed by thin layer chromatography (TLC), high pressure liquid chromatography (HPLC), and gas chromatography using a thermal energy analyzer (GLC-TEA). HPLC revealed the presence of n-nitrosodimethylamine (NDMA) (2 ug/g tobacco), N-nitrosohydroxyproline (NHPRO) (1 ug/g), as well as N-nitrosopyrrolidine (NPYR) and n-nitrosonornicotine (NNN). GLC-TEA confirmed the presence of NDMA (2-3 ug/g), NPYR (1-2 ug/g), and NNN (1 ug/g). The presence in tobacco of substances known to cause cancer in laboratory animals suggests the need for further research on their effects on habitual users of chewing tobacco and a possible relationship to cancer of the upper digestive tract in humans. (21 Refs)

OTHER ETIOLOGIC FACTORS IN GI CARCINOGENESIS

20. DOES PEUTZ-JEGHERS SYNDROME PREDISPOSE TO GASTROINTESTINAL MALIGNANCY? A LATER LOOK.

Linos DA, Dozois RR, Dahlin DC, Bartholomew LG
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Arch Surg; 116(9):1182-1184 1981

Several reports have recently suggested an association between the development of intestinal carcinoma and the presence of Peutz-Jeghers syndrome. During the 45-yr period between 1935 and 1979, 48 patients with Peutz-Jeghers syndrome were seen at the Mayo Clinic, Rochester, Minnesota, and followed up for a median period of 33 yr. Carcinoma of the small or large intestine did not develop in any patient, with possibly one exception. Survival of patients with Peutz-Jeghers syndrome also was found to be similar to that of the general population. Therefore, skepticism continues about the premalignant potential of this rare syndrome, especially in the small intestine, and surgical conservatism should be practiced in its management. (Author abstract) (18 Refs)

21. OCCURRENCE OF IN VITRO TETRAPLOIDY IN THE HERITABLE COLON CANCER SYNDROMES.

Danes BS
New York Hosp.-Cornell Medical Center, 525 E. 68th St., New York, NY, 10021
Cancer; 48(7):1596-1601 1981

Increased in vitro tetraploidy occurred in skin cultures derived from all affected patients and some family members at risk studied in families with heritable colon cancer syndromes (15 of 16 Gardner syndrome families, three Oldfield syndrome families, and four families with heritable colon cancer syndrome without polyposis coli) but was not present in all (one Gardner syndrome family, 16 of 19 familial polyposis coli families, and two Turcot syndrome families). Seven of 97 controls, family members by marriage, showed increased in vitro tetraploidy. None of these seven had a family history of colonic cancer but four had a family history of other solid tumors. Such in vitro studies illustrated that the occurrence of in vitro tetraploidy should be determined in families rather than individuals in order to determine whether all patients clinically affected show increased in vitro tetraploidy and vertical transmission that can be documented. (Author abstract) (21 Refs)

22. CHOLECYSTECTOMY AND CANCER OF THE LARGE BOWEL.

Turnbull PR, Smith AH, Isbister WH
(c/o Isbister) Dept. Surgery, Wellington Clinical Sch. Medicine, Wellington, New Zealand
Br J Surg; 68(8):551-553 1981

A matched case control study was conducted in order to determine the association between previous cholecystectomy and the development of large bowel cancer. One hundred and sixty men and 145 women presenting with large bowel cancer were studied. One control was selected for each case matched according to age, sex and date of admission. The medical records for each patient in the study were reviewed for evidence of previous cholecystectomy. No association was found among male patients, but for women an estimate of relative risk of 2.7 was obtained for patients who had had previous cholecystectomy. This association was largely a consequence of the fact that 10 female patients with rectal cancer had had a previous cholecystectomy compared with only 1 of their controls. It is possible that carcinogenic breakdown products of bile salts are most concentrated in the distal portion of the large bowel, but it is difficult to explain why the association should be confined to women only. (Author abstract) (24 Refs)

23. SECOND RESPIRATORY AND UPPER DIGESTIVE TRACT CANCERS AFTER ORAL CANCER.

Tepperman BS, Fitzpatrick PJ
Dept. Radiation Oncology, Princess Margaret Hosp., Ontario Cancer Inst., Univ. Toronto, Toronto, Canada
Lancet; 2(8246):547-549 1981

Between 1958 and 1975, 377 patients with squamous cell carcinoma of the floor of the mouth were treated. One hundred twenty-three new cancers (not recurrences) developed in 101 (27%) of these patients after treatment. Eighty-two (67%) were squamous cell carcinomas of the respiratory and upper digestive tracts, one-third of these being in the mouth. These tumors developed at a constant rate of 3.6% per yr and led to an excess mortality of 5.2% per yr. Men with oral cancer have a relative risk of 13.4 for new tumors in the upper respiratory and upper digestive tracts compared with the general population; in females the relative risk for all sites is 82.6. All patients with mouth cancer should thus be examined regularly because of this high risk of new cancers. (Author abstract) (19 Refs)

24. PERSPECTIVES FOR THE GENETIC STUDIES OF GASTROINTESTINAL NEOPLASMS.

Klimenkov AA, Sel'chuk VIu, Chudina AP
All-Union Cancer Res. Center, Moscow, USSR
Vestn Akad Med Nauk SSSR; (7):49-52 1981

Literature data on the role of genetic factors in the etiology of gastrointestinal neoplasms are reviewed. Genetical factors play a leading role in familial intestinal polyposis, Gardner's syndrome, Peutz-Jeghers syndrome, and juvenile polyposis. These diseases are transmitted as an autosomal dominant trait with high penetrance. Predisposition to familial adenocarcinomatosis and esophageal carcinoma with tylosis are transmitted as simple Mendelian traits. Environmental factors play a leading role in the etiology of vast majority of gastrointestinal neoplasms. The objective of genetical research of these neoplasms is to evaluate the characteristic features of the karyotype, to determine the role of HLA-system, and to elucidate the clonal origin of tumors. (14 Refs) (In RUS)

25. PREMALIGNANT AND MALIGNANT EPITHELIAL CHANGES IN THE ANTETHORACIC SKIN TUBE AFTER ESOPHAGOPLASTY.

Petri A, Petri I, Nemeth A, Imre J
I. Sebeszeti Klinika, Postafiok 464, H-6701 Szeged, Hungary
Chirurg; 52(8):501-504 1981

Seven patients required reoperation for premalignant and malignant epithelial changes in antethoracic skin tubes inserted for esophagoplasty 14-41 yr (av 30 yr) before for corrosive stricture of the esophagus due to ingestion of lye. Early superficially infiltrating squamous epithelial carcinoma, papillomatous epithelial hyperplasia with incipient malignant transformation, papillomatous epithelial hyperplasia with superficial invasion, partly keratinizing epidermoid carcinoma, pseudoepitheliomatous epithelial hyperplasia and chronic inflammation, papillomatous changes, chronic inflammation without signs of malignancy, and chronic inflammation with fibrosis without signs of malignant transformation were diagnosed histologically. These changes are assumed to have been caused by chronic inflammation due to chemical irritation of the skin tube by stagnant food, saliva, and gastro-neo-esophageal reflux. Based on personal experience and on data in the literature, it is suggested that the use of a skin tube in the repair of the esophagus should be reserved for the small group of patients with esophageal malignancy not amenable to other methods of reconstruction. (15 Refs) (In GER)

26. CHOLECYSTECTOMY AND COLON CANCER.

Svastits E, Ulyok Z, Besznyak I, Ihasz M

Sebeszeti Osztaly, Orszagos Onkologiai Intezet, Budapest, Hungary

Orv Hetil; 122(31):1889-1890 1981

The possible relationships between cholecystectomy and colorectal cancer were studied. Colorectal cancer was diagnosed in a series of 589 patients (283 women and 306 men) during a 10-yr period. The anamnestic data revealed cholecystectomy preceding the diagnosis of colorectal carcinoma by at least 2 yr in 25/589 patients (in 17/283 women and 8/306 men). Previous cholecystectomy was found in the anamnestic data of 12 patients in another series of 386 patients with colorectal cancer during a 10-yr period. The findings fail to suggest cholecystectomy to be a predisposing factor for colorectal cancer, as was indicated by data in the literature. (12 Refs) (In HUN)

27. NITROSABLE DRUGS.

Ziebarth D

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Arch Geschwulstforsch; 51(7):587-595 1981

The nitrosation of 61 potentially nitrosable drugs available for po administration in East Germany was studied in vitro under simulated conditions of the human stomach. Nitrosation of 10/61 drugs (aminophenazone, ampicillin, clomipramine, desipramine, ethambutol, imipramine, noramidopyrine methanesulfonate, oxacillin, phenoxymethylpenicillin, and piperazine) was observed. Nitrosodimethylamine, the principal product of aminophenazone, and mononitrosopiperazine, the principal product of piperazine, were identified chemically among the nitrosation products of the drugs. Both metabolites are carcinogenic for several animal species. The nitrosation of 9/10 drugs were inhibited 80-100% by ascorbic acid, and that of ampicillin by 18.2%. The findings indicate that po administered drugs forming carcinogenic N-nitroso compounds should be replaced by non-nitrosable drugs, and other potentially nitrosable drugs should be formulated with ascorbic acid, if they are compatible with this vitamin. (33 Refs) (In GER)

INDUCTION OF GI CARCINOGENESIS IN ANIMALS

28. CONTRIBUTION OF THE STUDY OF EXPERIMENTAL CANINE GASTRIC CARCINOMA TO THE STUDY OF HUMAN GASTRIC CARCINOMA.

Kurihara M, Izumi T, Shirakabe H, Okui K, Miyazaka K, Maruyama S, Sasaki Y, Inaguma H, Kamano Y, Yasui A, Suwa B

Third Dept. Internal Medicine, Saitama Medical Sch., Saitama 350-04, Japan

I To Cho; 16(7):737-744 1981

Induction of experimental gastric carcinoma in dogs by N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG) soln was investigated, and the dynamics of 5-fluorouracil (5FU) and uracil + 5-fluoro-1-(tetrahydro-2-furyl)-uracil (UFT) were studied in dogs bearing cancers. Gastric carcinomas were induced easily in the dogs by administering ENNG po 2x/day (13.8-23.8 g total) with food pellets, but scirrhous type gastric carcinoma was rarely induced with ENNG alone. On the other hand, 3/10 beagles given ENNG and gastrin developed scirrhous type carcinoma; all three tumors were observed in the pyloric and antrum regions of the stomach and were poorly differentiated adenocarcinomas. Signet ring cell carcinoma in the submucosa and marked proliferation of collagen fibers in the antrum were also observed. After iv injection and po administration of 14C-5FU to the ENNG-induced tumor-bearing dogs, higher concentrations of 5FU were observed in the cancer tissues (both superficial and deep) than in the normal tissues. Similar tests of UFT in a dog with ENNG-induced gastric carcinoma showed that 5FU concentrations were higher in the stomach and lungs than other tissues. (25 Refs) (In JPN)

29. PRODUCTION OF BORRMANN TYPE 3 GASTRIC CANCER IN DOGS TREATED WITH LOW CONCENTRATIONS OF ENNG.

Fujita M, Nampei S, Tsukahara Y, Taguchi T, Sato M

Dept. Surgery, Res. Inst. for Microbial Diseases, Osaka Univ., Osaka, Japan

I To Cho; 16(7):761-767 1981

Endoscopic, radiographic, and histologic examinations of gastric cancers induced in 8/15 dogs by means of low concentrations of N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG; 50 ug/ml/day; 3.4-9 .2 g total) administered for 30-52 wk were performed. Of the eight dogs that had gastric carcinoma, seven died of advanced gastric cancer up to 5 yr after initiation of the experiment. The primary tumor nests were Stage I in one case, II in one, III in one, and IV in four. Six of the dogs developed Borrmann Type 3 cancer from poorly-differentiated adenocarcinoma; serial examination of these tumors indicated that the primary tumor nests developed from Type IIc early stage carcinoma. Examination of the Borrmann Type 3 lesions showed limited cancerous spread in the mucosal layer, signet-ring cell cancer limited to small areas around the ulcer, diffuse infiltration of the submucosal layer, and invasion of poorly-differentiated adenocarcinoma to the serosa. Results indicated that this animal model can be used to study human gastric carcinoma. (16 Refs) (In JPN)

30. CANINE GASTRIC CARCINOMA AS AN ANIMAL MODEL OF HUMAN GASTRIC CARCINOMA.

Matsukura N, Morino K, Ohgaki H, Kawachi T
Div. Biochemistry, Natl. Cancer Center Res. Inst., Tokyo 104, Japan
I To Cho; 16(7):715-722 1981

Conditions needed to induce gastric cancer in dogs which resembles that found in humans were investigated, and the advantages of canine experimental gastric cancers as models were discussed with respect to human gastric cancer. Gastric carcinoma was induced in 15/15 male beagles that were given N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG; 100 or 150 ug/ml drinking water) for 5-9 mo. The eight dogs given 100 ug/ml of the ENNG primarily developed depressed-type early gastric carcinoma and Borrmann Type 2 or 3 advanced gastric carcinomas of the gastric angle and antrum. The seven dogs given 150 ug/ml of the ENNG primarily developed protruded or depressed-type early gastric carcinoma, Borrmann Type 1-like carcinomas and Type 3 advanced gastric carcinomas of the gastric angle, antrum, and a few on the corpus. Labeling indices (LIs) of canine gastric carcinoma were examined in vivo with pulse injection of methyl-3H thymidine iv. The LIs of cancerous lesions were lower than those of noncancerous gastric mucosa or that of untreated dogs. The LIs differed according to histological types of tumors and to the area of the particular lesion. Canine gastric cancers were thought to be valuable models for basic research on carcinogenesis and chemotherapeutic regimens. (10 Refs) (In JPN)

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31. EXPERIMENTAL CANINE GASTRIC CANCER AS A MODEL FOR HUMAN GASTRIC CANCER. COMPARISON OF HUMAN AND EXPERIMENTAL CANINE GASTRIC CANCERS.

Nakamura Y
Dept. Basic Medical Pathology, Tsukuba Univ., 1-1-1 Tendamadai, Sakura-mura, Niihara-gun, Ibaraki Prefecture 305, Japan
I To Cho; 16(7):723-726 1981

The question of whether or not experimental canine gastric cancers can be used as models for human gastric cancers was explored by examining and comparing the findings of research on both types of cancer. Biological and chemical similarities of human gastric cancer and canine gastric cancer such as the fact that both hosts are mammalian and have a great many metabolic pathways in common were considered to indicate that the existing cancer would have a similar host environment in either animal. On the other hand, intestinal metaplasia has been observed in human stomachs while it has not been observed in dogs, thus canine gastric cancer cannot be used as a model for human gastric cancer unless the cancer is a solid mucosal carcinoma. On the macroscopic level, the incidence of gastric cancers spontaneously occurring in the area of the pyloric gland, antrum, and even the lesser angle of the stomach was lower among the chemically induced canine cancers than the human cancers. Differences in the incidences of multiple gastric cancers also existed between the cases of human gastric cancer and induced, experimental canine cancers. Although many similarities exist between human and canine cancers, the histological difference between the two with respect to carcinogenesis of the mucosa is a major reason why the canine gastric cancer cannot be used as a model of the overall structure of human gastric cancer. (17 Refs) (In JPN)

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32. CARCINOGENESIS IN SYRIAN HAMSTERS BY N-NITROSO-2,6-DIMETHYLMORPHOLINE, ITS CIS AND TRANS ISOMERS, AND THE EFFECT OF DEUTERIUM LABELING.

Rao MS, Scarpelli DG, Lijinsky W
Dept. Pathology, Northwestern Univ. Medical Sch., 303 East Chicago Ave., Chicago, IL, 60611
Carcinogenesis; 2(8):731-735 1981

Syrian golden hamsters were divided into groups of 20 each. They were given doses of N-nitroso-2,6-dimethylmorpholine (NDMM), its cis or trans isomer, or its alpha-d4 or beta-d2 deuterium-labeled derivatives. The weekly doses (mg/kg body wt) were NDMM 18 or 50; cis-NDMM 11.5 or 31; trans-NDMM 6.5 or 17; d4 18 or 50; d2 50. A total of 52 benign and 21 malignant tumors resulted, most associated with the pancreas, liver, respiratory system, and kidneys. The survival rate among hamsters treated with cis-NDMM was about the same as the rate for those treated with NDMM. The survival rate with trans-NDMM was higher, indicating that trans-NDMM was a less potent carcinogen. Treatment with d4 produced tumors earlier than treatment with d2, suggesting that d4 was the more potent of the two. The overall incidences of malignant tumors for the NDMM, d4, and d2 groups were not significantly different. Activation to mutagenicity by pancreas microsomes, and binding to DNA of the pancreas did not differ between the isomers. (21 Refs)

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33. EXPERIMENTAL CANINE GASTRIC CARCINOMA AS A MODEL TO STUDY EFFECTS OF ANTICANCER DRUGS.

Tanaka Y, Uosumi G, Inokuchi H, Aoike A, Kawai K
Dept. Preventive Medicine, Kyoto Prefectural Univ. Medicine, Kyoto 602, Japan
I To Cho; 16(7):745-750 1981

Experimental gastric carcinomas were induced in eight beagle dogs by means of N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG), and the effects of a schizophyllum polyglucan (SPG) on the cancers were studied. Ten dogs were divided into four groups: Groups I (3 dogs), II (3), and III (2) were administered the ENNG, and Group IV (2) was not; Groups I and II were given SPG (2 mg/kg/wk) + Freund's incomplete adjuvant (FIA), while Group III was given NaCl + FIA and Group IV was given NaCl alone. The SPG was administered sc in all groups. Group I dogs were given the SPG 12 mo after administration of the ENNG and after cancerous lesions were observed. Group II dogs were given the SPG 5 mo after administration of the ENNG and while no cancerous lesions were observed. Changes in mitogen responses of peripheral lymphocytes from the dogs to concanavalin A and phytohemagglutinin were not observed in the dogs administered SPG, but the dogs not administered the SPG showed decreased mitogen response. However, as endoscopic examination of the cancers in the dogs given the SPG showed advancing growth of the tumors, therapeutic effect was doubted. The canine gastric cancer model was thought to be applicable for immunotherapy studies of human gastric cancers. (12 Refs) (In JPN)

34. EXPERIMENTAL CANINE GASTRIC CANCER AS A MODEL OF HUMAN GASTRIC CANCER: A SYMPOSIUM.

Nagayo T, Tsugimura T, Kawachi T, Yoshisawa S, Koyama S, Fukutomi H, Nakamura Y, Hachio T
Aichi Prefecture Cancer Res. Center Inst., Nagoya, Aichi Prefecture, Japan
I To Cho; 16(7):768-780 1981

The issue of whether or not the experimental canine gastric cancer is a suitable model for the study of human gastric cancer was explored. Included in the discussion was a review of the history of research on induction of gastric cancer in dogs with various chemicals, an examination of the merits and demerits (eg time and space requirements) of the canine gastric cancer as a model, an examination of the fact that intestinal metaplasia is not usually observed in association with canine gastric cancer, and applications of the canine model to clinical and therapeutic research on gastric cancer. (no Refs) (In JPN)

MECHANISMS AND MODIFICATIONS OF GI CARCINOGENESIS

35. NUTRITIONAL MODULATION OF CANCER.

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Dept. Nutrition and Food Science, Massachusetts Inst. Technology, Cambridge, MA, 02139
Cancer Detect Prev; 3(2):367-417 1981

A review is made of (1) specific target organs where epidemiologic and experimental animal data indicate a role for nutrition in tumor development, (2) the role of certain vitamins, especially vitamin A and ascorbic acid, in modulation of cancer, and (3) experimental evidence for a nutritional role in the modification of carcinogen metabolism and the host immune response. Nutritional deficiencies are etiologic factors in esophageal and gastric cancer, malnutrition and dietary carcinogens etiologic factors in liver cancer, and dietary fats etiologic factors in colon cancer. Dietary components that inhibit the metabolic activation of carcinogens include flavones, indoles, and antioxidants. Vitamin A and its synthetic analogs are effective inhibitors of carcinogen-induced epithelial neoplasms; they also enhance cellular immunity and antitumor response. (140 Refs)

36. EFFECT OF MAJOR SMALL BOWEL RESECTION ON DIMETHYLHYDRAZINE-INDUCED BOWEL CARCINOGENESIS.

Harte PJ, Steele G, Rayner AA, Munroe AE, King VP, Wilson RE
(c/o Steel) Brigham and Women's Hosp., 75 Francis St., Boston, MA, 021151
J Surg Oncol; 18(1):87-93 1981

We have investigated the effect of distal small bowel resection on chemically induced tumors of the gastrointestinal tract in Wistar/Furth (W/Fu) rats. Dimethylhydrazine (DMH) (20 mg/kg sc once wk x 16) was commenced 3 mo after rats underwent resection of the distal 30 cm of small bowel (1/3 resection) or after sham small bowel resection (controls). Fifty wk after the start of DMH administration, tumors were found in 15 of 25 animals who underwent small bowel resection compared to 9 of 31 animals in the control group (p less than 0.05). After small bowel resection, 8 of 15 tumors occurred at the site of anastomosis but no anastomotic tumors were seen after sham resection. In addition, tumors were larger and more invasive after small bowel resection. These data indicate that major small bowel resection potentiates DMH induced-intestinal carcinogenesis. (Author abstract) (28 Refs)

37. INHIBITION OF N-NITROSAMINE FORMATION BY SOYA PRODUCTS.

Kurechi T, Kikugawa K, Fukuda S, Hasunuma M

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Food Cosmet Toxicol; 19(4):425-428 1981

The soya products Tofu (soya bean curd), Miso (soya bean paste), soya milk without additives, and Bonlact (powdered soya milk with linoleic acid, vitamins, and minerals added) were tested at pH 3, 4, and 5. Known amounts of the soya products were added to reaction mixtures containing sodium citrate buffer (pH 3 or 4) and $NaNO_2$. All of the products tested reduced the levels of nitrite in the reaction mixtures. Reductions were faster at pH 3 than at pH4 and were dependent on the amount of soya product present. The most potent product was Miso, followed by Bonlact, Tofu, and soya milk, in order. Soya products were added to mixtures of $NaNO_2$ and dimethylamine or $NaNO_2$ and diethylamine. All products inhibited the formation of N-nitrosodimethylamine with greatest inhibition at pH 3. The most potent product was Bonlact, followed in order by Miso, Tofu, and soya milk. The in vitro results suggest that soya products may inhibit the formation of the potential carcinogens, the n-nitrosamines, in the stomach. The component(s) which causes the inhibition is not known. It may be either the unsaturated fatty acid component of the lipids or any of a variety of phenolic compounds. (19 Refs)

38. ASCORBIC ACID AND CANCER OF THE DUODENUM. AN EXPERIMENTAL STUDY.

Werner B, Denzer U, Mitschke H, Brassow F

Abteilung fur Allgemeinchirurgie, Universitat, Martinistrasse 52, D-2000 Hamburg 20, W. Germany

Langenbecks Arch Chir; 354(2):101-109 1981

The effect of vitamin C (administered po as sodium ascorbate, 2-3% in feed) on carcinoma of the small intestine induced by N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG: 120 mg/liter in drinking water) was studied in male Wistar rats. Group I was treated with ENNG only, Group II with ENNG and vitamin C simultaneously, and Group III with vitamin C only. The duration of each experiment was 18 wk. The number of tumor-bearing animals was 33/36 in Group I, 32/35 in Group II, and 0/10 in Group III. The total number of tumors was 156 in Group I and 136 in Group II. Gastric tumors were found in one animal in Group I and in three in Group II. The number of suprapapillary duodenal tumors was 88 in Group I and 96 in Group II, that of intrapapillary duodenal tumors 62 in Group I and 37 in Group II. Five jejunal tumors were found in Group I. Adenoma and borderline lesions were found in 4/36 animals in Group I and in 8/35 in Group II. The depth of carcinoma infiltration corresponded to Stage P2 in 1/36 animals in Group I and in 8/35 in Group II, to Stage P3 in 3/36 and 3/35 animals in Groups I and I respectively, and to P4 in 25/36 animals in Group I and in 13/35 animals in Group II. The findings indicate that vitamin C did not suppress tumor induction, but caused a change in the distribution of the small intestinal tumors according to localization, and a significant reduction (p less than 0.005) in the frequency of Stage P4. (20 Refs) (In GER)

39. EFFECTS OF 2-AND 3-TERT-BUTYL-4-HYDROXYANISOLE ON GLUTATHIONE S-TRANSFERASE AND EPOXIDE HYDROLASE ACTIVITIES AND SULFHYDRYL LEVELS IN LIVER AND FORESTOMACH OF MICE.

Lam LK, Sparnins VL, Hochalter JB, Wattenberg LW
Dept. Lab. Medicine and Pathology, Univ. Minnesota, Minneapolis, MN, 55455
Cancer Res; 41(10):3940-3943 1981

Butylated hydroxyanisole, a food additive, has been found to inhibit the neoplastic effects of a wide variety of chemical carcinogens. The commercially available preparations of butylated hydroxyanisole contain two isomers, 2-tert-butyl-4-hydroxyanisole (2-BHA) and 3-tert-butyl-4-hydroxyanisole (3-BHA). Both isomers induce increased activities of glutathione (GSH) S-transferase and epoxide hydrolase and increase acid-soluble sulfhydryl concentration in hepatic and forestomach tissues of A/HeJ mice. The inductions were assayed after 2 wk of feeding diets containing the two isomers. 3-BHA induced an increase in t he activity of hepatic microsomal epoxide hydrolase by 1.4x that of the control. The activity of cytosol GSH S-transferase was enhanced by both isomers. In the liver, the 3-BHA induction was more than 3x higher than that of 2-BHA. In the forestomach, however, the induction effect of the two isomers was reversed. The overall magnitude of the induction was much lower in the forestomach than in the liver. Synergistic effects on the induction of GSH S-transferase activity were observed in the forestomach cytosol when mixtures of different proportions of the two isomers were added to the diet. Max enzyme activity was obtained at a ratio of 75% 2-BHA and 25% 3-BHA. No synergistic effect was observed with the corresponding hepatic cytosolic enzyme. The relative inductive effects of 2-and 3-BHA on the acid-soluble sulfhydryl level of liver and forestomach tissues followed closely those on GSH S-transferase activity. The results of the present study show that the two isomers of butylated hydroxyanisole differ in the magnitude of their effects on carcinogen-metabolizing systems of the liver and forestomach. (Author abstract) (27 Refs)

BIOCHEMICAL, MORPHOLOGICAL AND IMMUNOLOGICAL ASPECTS OF GI CARCINOGENESIS

40. UTILIZATION OF BLOOD ANALYSES TO EVALUATE METABOLIC CHANGES IN CONTROL AND 1,2-DIMETHYLHYDRAZINE-TREATED ADULT MALE FISCHER RATS.

Southern JT, Schiller CM
(c/o Schiller) Lab. Organ Function and Toxicology, Natl. Inst. Environmental Health Sciences, P. O. Box 12233, Research Triangle Park, NC, 27709
Cancer Lett; 14(1):47-54 1981

Seven-wk-old male Fischer rats received 1,2-dimethylhydrazine hydrochloride (DMH: 35 mg/kg) by intubation and were examined 1.5 yr later for tumor incidence at which time blood analyses were performed. The incidence of tumors in the treated animals was 78%, while no tumors were seen in controls. Most of the tumors were in the colon. There were statistically significant differences between treated and control animals in total WBC, percentage of lymphocytes, and in the percentage of eosinophils and segmented cells. Treated animals had a lower lymphocyte number and an elevated level of polymorphonuclear WBC. Treated animals had decreases in serum Na and K and increase in phosphate; the ion balance of treated animals was decreased. Serum albumin levels were significantly elevated, total protein levels were lower, SGOT and SGPT levels were decreased and creatine phosphokinase level was elevated in treated animals. The albumin/globulin ratio was increased 3.5-fold in the treated animals. Creatinine concentration was decreased in the treated animals. These data obtained using routine hematoplasia analysis and biochemical analysis with the Sequential Multiple Analyzer Computer Multitest system indicate that the routine clinical analyses as performed with these techniques can be readily adapted to evaluate samples from laboratory animals. (29 Refs)

41. IN VIVO KINETICS OF O(6)-METHYLGUANINE AND 7-METHYLGUANINE FORMATION AND PERSISTENCE IN DNA OF RATS TREATED WITH SYMMETRICAL DIMETHYLHYDRAZINE.

Herron DC, Shank RC
(c/o Shank) Dept. Community and Environmental Medicine, Univ. California Coll. Medicine, Irvine, CA, 92717
Cancer Res; 41(10):3967-3972 1981

The rates of appearance and removal of 7-methylguanine and O6-methylguanine in DNA from rat liver, kidney, and colon were determined at various intervals up to 120 hr after ip administration of 10.2, 40.7, 81.5, or 163 mg 1,2-dimethylhydrazine (SDMH) per kg body wt (1/16, 1/4, 1/2, or 1 50% lethal dose) using high-pressure liquid chromatography and fluorescence spectrophotometry. In most cases, increasing doses of SDMH slowed the rate of methylation of DNA, especially of the liver; colon DNA was methylated at a faster rate than was liver DNA, and kidney DNA was methylated at the slowest rate following SDMH administration. Removal of O6-methylguanine was slow (half-life, 37 to 50 hr) when this base was present in liver DNA at concentrations above 400 umol/mol guanine; as the concentration fell below 300 umol O6-methylguanine per mol guanine, the removal rate more than doubled (half-life, 16 to 19 hr). Some evidence was obtained to suggest that in the first 12 hr after max DNA methylation following SDMH administration, a rapid time-dependent removal of 7-methylguanine from liver and kidney but not colon DNA occurred. In these instances, then, the rates of formation and removal of aberrant methylated bases did not follow first-order kinetics. (Author abstract) (33 Refs)

42. PRODUCTION OF ALPHA-FETOPROTEIN, NORMAL SERUM PROTEINS, AND HUMAN CHORIONIC GONADOTROPIN IN STOMACH CANCER: HISTOLOGIC AND IMMUNOHISTOCHEMICAL ANALYSES OF 35 CASES.

Kodama T, Kameya T, Hirota T, Shimosato Y, Ohkura H, Mukojima T, Kitaoka H
Pathology Div., Natl. Cancer Center Res. Inst., 5-1-1, Tsukiji, Chuo-ku, Tokyo 104, Japan
Cancer; 48(7):1647-1655 1981

By immunoperoxidase histochemical staining of formalin-fixed paraffin-embedded sections, the production of alpha-fetoprotein (AFP), albumin (ALB), transferrin (TF), alpha-1-antitrypsin (AAT), and human chorionic gonadotropin (HCG) was examined in 35 operatively resected stomach cancers with elevated serum AFP levels (higher than 20 ng/ml as determined by radioimmunoassay). Cells positive for AFP were found in 19 cases (54%). In 29 cases (83%), some tumor cells contained normal serum proteins (ALB, TF, or AAT). All 19 tumors with AFP-positive cells also stained positively for two or three kinds of normal serum proteins. In some cases, AFP and normal serum proteins were localized in the same cells. There were two cases in which metastatic tumors produced AFP, whereas the primary sites did not. In nine cases (26%), HCG was present in tumor cells and HCG- and AFP-positive cells were coexistent in six tumors. Histologic examination of AFP-producing stomach tumors revealed medullary or papillotubular arrangements with marked nuclear atypia and eosinophilic granular or clear cytoplasms containing no glycogen or mucin. Some tumors with medullary patterns resembled liver cell carcinomas. Concordant phenotypic expression of AFP and normal serum protein production appears to be a general feature of AFP-producing tumors such as liver cell carcinoma, yolk sac tumor, and stomach cancer. (Author abstract) (47 Refs)

43. ALTERATIONS IN SURFACE ULTRASTRUCTURE AND ANIONIC SITES OF RAT DIMETHYLHYDRAZINE-INDUCED INTESTINAL TUMORS.

Jacobs LR
Dept. Internal Medicine, Sch. Medicine, TB 192, Univ. California, Davis, CA, 95616
Virchows Arch [Cell Pathol]; 37(2):207-216 1981

The relative roles of cell surface shedding and electronegative charge as determinants of metastatic capacity were studied in experimentally produced intestinal tumors. The ultrastructural organization and distribution of anionic sites on the luminal plasma membrane surface components were examined in small intestinal and colonic tumors induced in male Sprague-Dawley rats with 1,2-dimethylhydrazine. The overall distribution of negatively charged groups was demonstrated with ruthenium red staining. Compared to normal epithelial cells, neoplastic cells revealed evidence of decreased cell surface shedding as manifested by decreased numbers of membrane-bound bodies, and an increased quantity of glycocalyx. Malignant cell surfaces were directly exposed to the intestinal lumen as a result of losing the enteric surface coat covering. The exposed microvilli appeared damaged with shortening and blunting. The glycocalyx and surface coat both reacted strongly with ruthenium red indicating the presence of anionic sites. As a result of surface coat loss, the malignant cell surface components revealed an overall decrease in net negative charge. These alterations in cell surface component ultrastructure and electronegative charge appear to be consistent with the low capacity for chemically induced rat intestinal tumors to metastasize. (Author abstract) (15 Refs)

44. CELL SURFACE ANTIGENS OF HUMAN RENAL CANCER DEFINED BY MOUSE MONOCLONAL ANTIBODIES: IDENTIFICATION OF TISSUE-SPECIFIC KIDNEY GLYCOPROTEINS.

Ueda R, Ogata S-I, Morrissey DM, Finstad CL, Szkudlarek J, Whitmore WF, Oettgen HF, Lloyd KO, Old LJ
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Proc Natl Acad Sci USA; 78(8):5122-5126 1981

Seventeen monoclonal antibodies derived from fusions with spleen cells of mice immunized with established culture lines of renal cancers identified 9 cell-surface antigenic systems. Six of the systems (gp160, S25, gp120r, gp120nr, gp115, and V1) represent antigens not previously described. the other three systems are related to HLA-A, -B, and -C heavy chain and A and B blood group antigens. The most restricted of the newly described antigens are gp160, S25, and gp120r. These determinants are found only on cells of renal origin, both normal and malignant, and represent differentiation antigens of human kidney. In addition to the difference in the mol wt of two of these antigens, gp160, S25, and gp120r can be distinguished on the basis of differential expression on a panel of cultured renal cancers and normal kidney epithelium and fetal kidney cells. Glycoproteins bearing gp120r share a determinant with renal gp120nr (as indicated by sequential precipitations with monoclonal antibodies that detect gp120r and gp120nr), but gp120nr is found on a broader range of cell types, including fibroblasts and cell lines derived from lung, bladder, and colon cancers. The two other new systems, gp115 and V1, have characteristics of broadly occurring differentiation antigens but can be distinguished from each other and from gp120nr by differences in mol wt, heat stability (V1 is a heat-stable determinant), and differential expression on cell types of diverse origin. (Author abstract) (9 Refs)

45. HEXOKINASE ASSAY IN BIOPSY SPECIMENS OF STOMACH NEOPLASMS.

Bassalyk LS, Liubimova NV
All-Union Cancer Res. Inst., Moscow, USSR
Vestn Akad Med Nauk SSSR; (7):52-55 1981

Activity and isoenzyme spectrum of hexokinase (HK) were studied in biopsy specimens from 64 patients with stomach neoplasms (50 had cancer and 14 had polyposis). Total HK activity in malignant tumors was 1.5-2x greater than that in the normal gastric mucosa and benign tumors. Characteristic feature of malignant tumors was increased content of HK-2 (32.9% in poorly differentiated carcinoma and 33.5% in adenocarcinoma, compared with 9.6% in gastric polyp and 4.8% in normal gastric mucosa). (8 Refs) (In RUS)

46. ANTIBODY-DEPENDENT CELL-MEDIATED CYTOTOXICITY IN X-IRRADIATION-INDUCED ADENOCARCINOMA OF THE RAT SMALL BOWEL.

Stevens RH, Cole DA
Radiation Res. Lab., 14 Medical Lab., Dept. Radiology, Univ. Iowa, Iowa City, IA, 52242
Radiat Res; 87(3):635-645 1981

The production of immunoglobulins during antibody-dependent cell-mediated cytotoxicity (ADCC) was studied in x-ray-induced adenocarcinomas in male outbred Holtzman rats. Approx 10-25% of the Holtzman rats, which had only their hypoxic small intestine exposed to the ionizing radiation developed small bowel adenocarcinomas that could be visibly detected, while of the remaining animals (75-90%), few (1-2%) developed identifiable lesions throughout their lifetimes. Positive ADCC was observed for both groups when peripheral blood lymphoid cells (PBLC) from unirradiated control animals were used as the effector cells. For the expression of the ADCC, both the serum-exposed rats and effector cells were found to be necessary for cytotoxicity. No apparent correlation was observed between the existence of visible cancer and the size of the lesion with the level of ADCC. The specificity of the ADCC responses was studied. Cytotoxicity was found to exist in the serum component. Among the majority of animals (75-90%) which had been exposed under identical conditions to the tumorigenic levels of x-rays but failed to develop the visible lesions, circulating immunoglobulins capable of inducing ADCC were found to be present. The serum immunoglobulins responsible for the antitumor immunity were of the IgG class. (39 Refs)

REVIEWS AND OTHER RELATED STUDIES

47. PROMOTION BY UNSATURATED FAT OF AZASERINE-INDUCED PANCREATIC CARCINOGENESIS IN THE RAT.

Roebuck BD, Yager JD, Longnecker DS, Wilpone SA
Dept. Pharmacology, Toxicology, Dartmouth Medical Sch., Hanover, NH, 03755
Cancer Res; 41(10):3961-3966 1981

Diet has been shown to modulate the incidence of a wide variety of chemically induced cancers in animals. Various diets fed either during the initiation stage or the postinitiation (promotion) stage of carcinogenesis were evaluated for their ability to modulate the incidence of pancreatic cancer. Male Wistar/Lewis rats were treated with multiple injections of the pancreatic carcinogen, azaserine, during a 6-to 7-wk-long initiation phase and were autopsied after a postinitiation phase of 34 or 44 wk. The following diets were evaluated for their effects on the incidence of pancreatic neoplasms during each stage of carcinogenesis: high saturated fat; two high unsaturated fats (corn oil and safflower oil); low protein; and caloric restricted. A purified control diet was fed during that stage when the test diets were not fed. The incidence of pancreatic adenomas and adenocarcinomas was evaluated by light microscopy. Feeding of the caloric-restricted diet during the initiation phase suppressed the pancreatic neoplasm incidence. None of the other diets tested had an effect on the incidence of pancreatic cancer during the initiation phase. During the postinitiation phase, both high-unsaturated-fat diets but not the high-saturated-fat diet significantly elevated the pancreatic neoplasm incidence. The low-protein and caloric-restricted diets had no effect on the neoplasm incidence when fed during the postinitiation phase. Thus, diets high in unsaturated fat appear to promote pancreatic carcinogenesis in the azaserine-treated rat while a diet high in saturated fat failed to show a similar degree of enhancement of pancreatic carcinogenesis. (Author abstract) (42 Refs)

48. SEX DIFFERENCES IN THE EFFECTS OF RETINOIDS ON CARCINOGENESIS BY N-NITROSOBIS(2-OXOPROPYL)AMINE IN SYRIAN HAMSTERS.

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Cancer Lett; 14(1):13-21 1981

Male and female Syrian hamsters received a single dose of N-nitrosobis(2-oxopropyl)amine (BOP: 40 mg/kg, sc) and 1 wk later were fed one of four retinoid types (13-cis-retinoic acid (13-cis-RA), N-ethylretinamide (ERA), 2-hydroxy-ethylretinamide (OH-ERA), or 4-hydroxyphenylretinamide (PRA)) each at three dose levels reported as 0.05, 0.1, and 0.2 milliM/kg diet. The wt of the pancreas was influenced by the sex and retinoid level: wt increased in females fed the high retinoid level and decreased in males fed the 0.1 milliM level. Nearly all animals developed pancreatic adenomas. The av number of adenomas was reduced in female hamsters fed retinoids. The greatest decrease occurred with 13-cis-RA (48% reduction), with reductions intermediate for ERA and OH-ERA (39%), and smallest for PRA (14%). In male hamsters, pancreatic adenoma incidence was not influenced by retinoid treatment; however, the multiplicity of these lesions in males fed OH-ERA and PRA was greater than those fed 13-cis-RA, ERA, or control diet. The pancreatic carcinoma incidence was not influenced by retinoids, although female hamsters fed 13-cis-RA developed fewer carcinomas per animal than did animals fed ERA. In female, but not male, hamsters, the liver tumor incidence was reduced from 60% to 21% by feeding OH-ERA, and the gallbladder tumor incidence from 60% to less than 10% in females fed 13-cis-ERA and ERA. These results suggest that sex hormones or other sex differences may influence the factors which determine the ability of retinoids to inhibit carcinogenesis. (33 Refs)

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NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. TOXICOLOGICAL ASPECTS OF POLYCYCLIC AROMATIC HYDROCARBONS (PAH).
De Fernicola NA, De Azevedo FA
Divisao de Toxicologia e Ecotoxicologia, Diretoria de Tecnologia e Desenvolvimento, Sao Paulo, Brazil
Rev Bras Saude Ocup; 33(9):62-68 1981
In POR

2. EVALUATION OF THE CARCINOGENIC RISK OF CHEMICALS TO HUMANS: SOME ANTINEOPLASTIC AND IMMUNOSUPPRESSIVE AGENTS.
International Agency for Research on Cancer
International Agency for Res. on Cancer, Lyon, France
IARC Monogr Eval Carcinog Risk Chem Hum; 26:1-411 1981

3. STUDIES ON THE ROLE OF ORAL CONTRACEPTIVE USE IN THE ETIOLOGY OF BENIGN AND MALIGNANT LIVER TUMORS.
Mettlin C, Natarajan N
Cancer Control and Epidemiology, Rosewell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
J Surg Oncol; 18(1):73-85 1981

RADIATION CARCINOGENESIS

4. EXPERIMENTAL RADIATION CARCINOGENESIS: WHAT HAVE WE LEARNED?
Fry RJ
Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN, 37830
Radiat Res; 87(2):224-239 1981

5. INFLUENCE OF NONCARCINOGENIC SECONDARY FACTORS ON RADIATION CARCINOGENESIS.
Little JB
Lab. Radiobiology, Harvard Univ., Sch. Public Health, Boston, MA, 02115
Radiat Res; 87(2):240-250 1981

6. MEDICAL IRRADIATION IN JAPAN - STOCHASTIC RISK ESTIMATION AND ITS REDUCTION.
Hashizume T
Div. Physics, National Inst. Radiological Sciences, 9-1 Anagawa 4-Chome, Chiba Shi 260, Japan
Nipnon Igaku Hoshasen Gakkai Zasshi; 41(5):445-474 1981
In JPN

7. RADIOACTIVITY IN DRINKING WATER.
Cothern CR
Office of Drinking Water, Environmental Protection Agency, Washington, DC
Radioactivity in Drinking Water. Available from National Technical Information Service, Springfield, VA, as PB81-192833:, 79 pp., 1981.

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

8. EPIDEMIOLOGY OF GASTROINTESTINAL CANCER.
Miller AB
NCIC Epidemiology Unit, Univ. Toronto, McMurrich Building, Toronto, Ontario M5S 1A8, Canada
Compr Ther; 7(8):53-58 1981

9. EPIDEMIOLOGICAL ASPECTS OF ESOPHAGEAL CANCER.
Ruggieri M, Tosato F, De Rocco K, Lepore M, Cipriano E, Paolini A
IV Cattedra di Clinica Chirurgica Generale e Terapia Chirurgica, Universita degl i Studi di Roma, Rome, Italy
Recenti Prog Med; 70(5):545-556 1981
In ITA

10. PANCREATIC CANCER.
Cohn I, Hastings PR
Dept. Surgery, Louisiana State Univ., 1542 Tulane Ave., New Orleans, LA, 70112
UICC Tech Rep Ser. Vol. 57, Issue 12, 142 pp., 1981.

11. GENETICALLY DETERMINED SUSCEPTIBILITY TO CANCER.
Marks PA
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Blood; 58(3):415-419 1981

12. ETIOLOGY, ROLE AND DETECTION OF CHROMOSOMAL ABERRATIONS IN MAN.
Fabricant JD, Legator MS
Dept. Preventive Medicine, Div. Environmental Toxicology, Univ. Texas Medical Branch, Galveston, TX, [illegible]550
JOM; 23(9):617-625 1981

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN CARCINOGENESIS

13. INDUSTRIAL CARCINOGENESIS.
Vickers CF
Dept. Dermatology, Univ. Liverpool, Liverpool L69 3BX, England
Br J Dermatol; 105(Suppl21):57-61 1981

14. ENVIRONMENT AND HEALTH (LITERATURE REVIEW).
Khachatrian TS
Dept. Public Health, State Inst. Advanced Training for Physicians, Erevan, USSR
Zh Eksp Klin Med; 21(3):287-292 1981
In RUS

15. LIFESTYLE AND CANCER.
Higginson J
International Agency for Res. on Cancer, Lyon, France
Cancer Forum; 5(1):4-14 1981

16. ASBESTOS, AN ENVIRONMENTAL POLLUTANT.
Zamfir G, Diaconu R
Institutul de igiena si sanatate publica, Iasi, Romania
Igiena; 30(1):1-9 1981
In RUM

17. REVIEW OF UICC PROGRAM ON SMOKING AND LUNG CANCER.
Gray N
Smoking and Cancer Program, UICC, 3 rue du Conseil General, 1205 Geneva, Switzerland
Cancer Forum; 5(1):15-18 1981

CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

18. EXPERIMENTAL APPROACHES TOWARDS THE BIOCHEMICAL ANALYSIS OF CHEMICAL CARCINOGENESIS.
Laishes BA
McArdle Lab. for Cancer Res., Univ. Wisconsin Medical Sch., Madison, WI, 53706
ACS Symp Ser; 160:197-215 1981

19. FIBRONECTIN AND RELATED TRANSFORMATION-SENSITIVE CELL SURFACE PROTEINS (ONCOLOGY OVERVIEW).
International Cancer Research Data Bank
ICRDB Program Office, NCI, Westwood Building, Room 10A18, Bethesda, MD, 20205
Fibronectin and Related Transformation-Sensitive Cell Surface Proteins (Oncology Overview) Chen, L. B, ed This Title is Available Through National Technical Information Service, Springfield, VA, as NTISUB/PB81-923001:; OB-81/01:95pp. 1981

20. PRENEOPLASTIC LESIONS OF THE MAMMARY GLAND. (ONCOLOGY OVERVIEW)
International Cancer Research Data Bank
ICRDB Program Office, NCI, Westwood Building, Room 10A18, Bethesda, MD, 20205
Preneoplastic Lesions of the Mammary Gland (Oncology Overview) Medina, D, ed This Title is Available Through National Technical Information Service, Springfield, VA, as NTISUB/PB81-923002; OB-81/02:134pp. 1981

21. LYMPHOCYTE DIFFERENTIATION: AN ESSENTIAL BASIS FOR THE COMPREHENSION OF LYMPHOID NEOPLASIA.
Magrath IT
Pediatric Oncology Branch, Div. Cancer Treatment, NCI, NIH, Public Health Service, United States Dept. Health and Human Services, Bethesda, MD, 20205
JNCI; 67(3):501-514 1981

MODIFICATION OF CARCINOGENESIS

22. FACTORS STIMULATING AND INHIBITING TUMOR GROWTH IN CARCINOGENESIS.
Kochergina NI, Kosova IP
Res. Lab. Experimental Immunobiology, Moscow, USSR
Usp Sovrem Biol; 91(3):409-418 1981
In RUS

23. TWO INDEPENDENT ASPECTS OF TUMOR PROMOTION.
Berenblum I, Armuth V
Weizmann Inst. Science, Rehovot, Israel
Biochim Biophys Acta; 651(1):51-63 1981

VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

24. BURKITT'S LYMPHOMA.
Ziegler JL
NCI, Bethesda, MD, 20205
N Engl J Med; 305(13):735-745 1981

25. REVIEW ARTICLE. REGULATION OF EXPRESSION OF THE INTEGRATED RETROVIRUS GENOME.
Weinberg RA, Steffen DL
Center for Cancer Res., Massachusetts Inst. Technology, Cambridge, MA, 02139
J Gen Virol; 54(part1):1-8 1981

METHODOLOGY IN CARCINOGENESIS RESEARCH

26. THE DEVELOPMENT AND VALIDATION OF MUTAGENICITY SCREENING TESTS.
Durkin PR, Santodonato J
Center for Chemical Hazard Assessment, Syracuse Res. Corporation, Merill Lane, Syracuse, NY, 13210
Tappi; 64(9):153-159 1981

27. SHORT-TERM TEST SYSTEMS FOR POTENTIAL MUTAGENS AND CARCINOGENS: I. MICROBIAL TESTS (ONCOLOGY OVERVIEW).
International Cancer Research Data Bank
ICRDB Program Office, NCI, Westwood Building, Room 10A18, Bethesda, MD, 20205
Short-Term Test Systems for Potential Mutagens and Carcinogens: I Microbial Tests (Oncology Overview) Simmon, V F; Peirce, V; eds This Title is Available Through National Technical Information Service, Springfield, VA, as NTISUB/PB81-922903:; OK-81/03:124pp. 1981

28. ANIMAL MODELS OF INTRA-ORAL CHEMICAL CARCINOGENESIS: A REVIEW.
Eveson JW
Dept. Oral Medicine and Pathology, Guy's Hosp., London SE1 9RT, England
J Oral Pathol; 10(3):129-146 1981

29. THE CHROMOSOMES IN HEMATOLOGY.
Berger R
Laboratoire de Cytogenetique, Institut de Recherches sur les Leucemies et les Maladies du Sang, UER d'Hematologie, Hopital Sant-Louis, 2 place du Dr. Fournier, 75475 Paris Cedex 10, France
Cancer Genet Cytogenet; 4(1):69-88 1981

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Gastrointestinal Tract and Pancreas

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service • National Institutes of Health • National Cancer Institute

HE 20. 3173/2:

PREVALENCE OF GI CANCER IN HUMAN POPULATIONS

1. INTERNATIONAL COMPARISON OF TRENDS IN CANCER MORTALITY FOR SELECTED SITES.

Hayakawa N, Kurihara M
Dept. Epidemiology and Social Sciences, Res. Inst. Nuclear Medicine and Biology, Hiroshima, Japan
Soc Sci Med [Med Geogr]; 15(1):245-249 1981

Trends in mortality rates due to cancer based on age adjusted death rates in 23 countries are reported to help elucidate causal factors. Annual variation in rates from 1954 to 1975 were calculated under the assumption that the mortality rates changed exponentially and the number of deaths followed the Poisson distribution. Results for males showed significant increases in 22 countries. Sites showing greatest increases were respiratory organs (5.9% to 0.9%) and intestine (3.9% to-4.0%). Results for females showed significant decreases. Sites with increased incidence of cancer included breast (1.8% to 0.2%) and intestine (4.1% to-0.7%), while uterine (-0.6% to-3.8%) and stomach (0.3% to-4.8%) cancers decreased. Specific countries showing large increases include Portugal with 0.3% to 0.8% increase in stomach cancer, and Italy with a significant increase in cancer of all sites except stomach. The 23 countries investigated are 'developed' countries; cancer death rates need to be studied in developing countries as well. (10 Refs)

2. MORTALITY FROM SELECTED MALIGNANT NEOPLASMS IN THE BRITISH ISLES: THE SPATIAL PERSPECTIVE.

Howe GM
Dept. Geography, Univ. Strathclyde, Glasgow, Scotland
Soc Sci Med [Med Geogr]; 15(1):199-211 1981

Standardized mortality ratios (SMRs) for cancer of the trachea, lung, bronchus, stomach, large intestine, and rectum in males and for breast cancer in females (both sexes, age 15-64 yr old) were calculated (1970-72 yr) for 320 administrative units in the United Kingdom. SMRs were also calculated for intestinal and rectal cancer in the Republic of Ireland. The SMRs are shown on demographic maps that demonstrate marked spatial variations in the mortality patterns of the selected neoplasms. Mortality from tracheal, bronchial, and lung cancer was highest in the London borough of Southwark, Glasgow, and Bootle in Lancashire. Gastric cancer mortality was high in North Wales and Scotland, and intestinal cancer mortality was elevated in Dublin, Belfast, and Aberdeen. The spatial distributions did support reported relationships between lung cancer and smoking, between gastric cancer and blood group A, or between intestinal cancer and carbohydrate-rich diets. (27 Refs)

3. COMPUTATION OF CANCER INCIDENCE RATES FOR DEFINED SMALL GEOGRAPHICAL AREAS - MATCHING OF NUMERATOR AND DENOMINATOR.

Pompe-Kirn V, Ravnihar B, Ferligoj A
Inst. Oncology, Univ. Ljubljana, 61105 Ljubljana, Yugoslavia
Neoplasma; 28(3):363-369 1981

The authors present the problem of validity of numerator and pertinence of denominator for small geographical areas in a sample of av annual crude incidence rates of stomach cancer in Slovenia during the period 1968-1974. At census in 1971 this country counted 1,727,137 of the population. According to the residence of the patients the rates have been calculated for 60 municipalities, and besides for 29 so called 'epidemiological regions', defined by their geographical and ethnic characteristics. Although in both instances great differences in incidence rates have been found, only a few area units exhibited a significantly lower or higher rate from the national av. Areas with small population base, 'disappeared' in the av, although the value of the rate for them was rather low or high. A formula is presented by which at a given rate for the total country it is possible to determine the minimal size of the population which still could provide estimation of a statistically significant lower rate. Thus, for areas with small population a period of observation through many yr is required in order to obtain the necessary minimal population base. The question is pointed out, whether this approach is reasonable as to the epidemiological interest, considering that some factors related to cancer may change during the long period of time. On the other hand, when merging small areas into larger ones, attention must be paid that these are not too heterogenous as to their cancer incidence rate, geographical, ethnic socio-economic and life-style features. (Author abstract) (6 Refs)

4. CANCER INCIDENCE IN QUEBEC (1971-1975) AND CARTOGRAPHY.

Thouez JP, Beauchamps Y, Dubois A, Simard A
Departement de geographie, Universite de Montreal, C.P. 6128, Montreal, Quebec, Canada
Union Med Can; 110(9):798-802 1981

A method is described for the geographic mapping of regional variations in the incidence of certain types of cancer observed in the province of Quebec between 1971 and 1975. Age-adjusted rates of cancer show a higher incidence of cancer in males. Cancer mortality rates in Quebec province have been found to be greater than those observed for Canada as a whole. The existence of artifical regional variations resulting from methods of data collection and analysis has been proposed. Geographic maps of standardized incidence ratios for breast, intestine, prostate, cervix, rectosigmoid, trachea, bronchi, and lungs cancers in the 74 federal counties of Quebec is presented. These representations indicated that cancers of trachea, bronchi, and lungs occur at similar rates in urban and rural areas. Breast cancer occurs more often in urban areas as compared with cervix cancer. Cancers of the rectum and intestine show similar geographical distributions. Prostate cancer shows many major geographic concentrations. (14 Refs) (In FRE)

5. CARCINOMA OF THE OESOPHAGUS IN NORTHERN TANZANIA (MEETING ABSTRACT).

Lauren PA, Jones ME
Department of Pathological Anatomy, University of Turku, Turku, Finland
Eighth European Congress of Pathology, August 30-September 4, 1981, Helsinki, Finland.

Within Northern Tanzania there is greater variation in incidence of esophageal carcinoma than for any other type of cancer. In 1972-79 177 new cases, 3.8% of 4692 malignancies registered, were seen, the patients coming from the eight administrative regions of Northern Tanzania with population of 4.9 million. The Mt Kilimanjaro area had a yearly incidence 3.9 for 10(5) males and 1.0 for females. These incidence rates are considerably higher than the rates in neighboring Uganda and most regions of Kenya. The highest relative frequency, 13.1% of all tumors and three x higher than in Mt Kilimanjaro area was seen in the coastal Tanga region. On the contrary, no or very few cases were seen from four of the inland regions. High risk regions had more male predominance, 8.5:1, than low risk regions, 3.8:1. The high risk Tanga region is the most important sisal production area of Tanzania with large number of laborers recruited from inland regions. Dominant tribes in Tanga region had proportionally less esophageal cancer than immigrated tribes. The role of more abundant alcohol consumption among immigrants as a possible causative factor of esophageal cancer is discussed. (no Refs)

6. ATLAS OF CANCER MORTALITY IN THE PEOPLE'S REPUBLIC OF CHINA. AN AID FOR CANCER CONTROL AND RESEARCH.

Li JY, Liu BQ, Li GY, Chen ZJ, Sun XD, Rong SD

Dept. Cancer Epidemiology, Cancer Inst. Chinese Acad. Medical Sciences, 2, Yabao Lu, Chaoyang, Qu, Beijing, People's Republic of China

Int J Epidemiol; 10(2):127-133 1981

A set of maps which display the patterns of cancer mortality in China has been prepared and published by the China Map Press. The 200 page atlas was edited by the National Cancer Control Office of the Ministry of Health and the Nanjing Institute of Geography of the Chinese Academy of Sciences on the basis of a nation-wide cancer mortality survey. The Cancer Institute of the Chinese Academy of Medical Sciences with related Colleges, Universities and Institutes provided the data and took part in the preparation of the atlas, which is published both in Chinese and English. Fifty eight maps and several dozen charts depict, in seven colors, the mortality distribution in the 2,392 counties and county-level administrative units of nine types of cancer common in China - stomach, esophagus, liver, cervix, lung, colon and rectum, breast, nasopharynx, and leukemia as well as five less common cancers - brain tumors, malignant lymphoma, cancer of the bladder, of the penis, and choriocarcinoma. The Atlas of Cancer Mortality will be an important new aid for cancer control and research in the People's Republic of China. (Author abstract) (10 Refs)

7. CANCER DEATHS BY CITY AND COUNTY IN JAPAN (1969-1971): A TEST OF SIGNIFICANCE FOR GEOGRAPHIC CLUSTERS OF DISEASE.

Ohno Y, Aoki K

Dept. Preventive Medicine, Nagoya Univ. Sch. Medicine, Nagoya, Japan

Soc Sci Med [Med Geogr]; 15(1):251-258 1981

The geographic distribution of esophageal, breast, and uterine cancer mortality by city and county in Japan was analyzed by a chi-square significance test. The test procedure included identification of all geographically adjacent areas, enumeration of observed adjacent concordant category pairs (accp), and calculation of expected accp. Areas with high esophageal cancer mortality were significantly clustered in both sexes, and those with low mortality were clustered in males. In the case of uterine cancer, significant aggregations were observed in areas with low or slightly high mortality rates. There was no significant aggregation for breast cancer. The validity of the chi-square test was confirmed by a Monte Carlo approach to Knox's test for space-time clustering. (11 Refs)

8. RECTAL CANCER INCIDENCE RATES FOR THE CITY OF MOSCOW.

Brusilovskii MI, Gritsman IuIa, Moshkov KV, Astrakhankina TA, Likhovetskaia LI, Zaseev VK

Res. Inst. Oncology and Municipal Oncological Dispensary, Moscow, USSR

Vopr Onkol; 27(8):65-68 1981

In 1975-1979, 5,369 cases of primary rectal tumors were registered in the City of Moscow, showing an increase in incidence rate from 11.9 to 15.7 and mortality rate from 4.6 to 6.1 per 100,000 of population, with patients being predominantly older than 60 yr. (Author abstract) (3 Refs) (In RUS)

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN GI CARCINOGENESIS

9. THE RELATIONSHIP BETWEEN MALIGNANCY AND FLUORINE CONTENT IN THE DRINKING WATER IN XILINKUOLEMENG, NEI MENGGU..

A L, Wang B

Bureau of Public Health, Xilinkuolemeng, People's Republic of China

Zhonghua Zhongliu Zazhi; 3(1):19-21 1981

Increased cancer mortality rates have been attributed to fluorine in drinking water. The relationship between malignancy and fluorine content in the drinking water of the Xilinkuolemeng district in northeastern Inner Mongolia is described. The fluorine contents in the drinking water of 10 countries within this distinct were determined and were found to range between 1.10 mg/l and 5.33 mg/l in 8 countries which exceeded the government limits of 0.5-1.0 mg/l. When the cancer mortality rates of the countries in this distinct were compared, a positive correlation was observed between fluoride content and cancer mortality rates, especially those of gastric, esophageal and brain cancer, in this district. In is concluded that high-fluorine content in the drinking water of Xilinkuolemeng may be one of the etiologic factions that contribute to the high incidence of certain malignant tumors in this district. (3 Refs) (In CHI)

10. CANCER AND THE PHYSICOCHEMICAL QUALITY OF DRINKING WATER IN QUEBEC.

Thouez JP, Beauchamp Y, Simard A

Dept. Geography, Univ. Montreal, Montreal, Quebec, Canada

Soc Sci Med [Med Geogr]; 15(1):213-223 1981

Epidemiologic studies of the carcinogenicity of drinking water are reviewed, and results of an investigation of the relationship between the quality of drinking water and cancer in Quebec a re presented. Standardized incidence ratios (SIRs) for gastrointestinal, urogenital and other neoplasms (1971-1975) were calculated for 46 Quebec census regions in which at least 50% of the population was supplied with drinking water from the St Lawrence river. Regions with high and low SIRs were compared according to the physicochemical characteristics of the drinking water. Correlation and regression analysis revealed a significant positive association between 'soft' water and the incidence of cancer of prostate, rectum, and digestive system organs. 'Hard' water was negatively associated with the incidence of stomach, prostate, and rectal cancer. (46 Refs)

11. CANCER AND DRINKING WATER IN LOUISIANA: COLON AND RECTUM.

Gottlieb MS, Carr JK, Morris DT
Dept. Medicine, Dept. Biostatistics and Epidemiology, Tulane Univ. Sch. Medicine, 1430 Tulane Ave., New Orleans, LA, 70112
Int J Epidemiol; 10(2):117-125 1981

A case-control mortality study conducted in 20 parishes (counties) of South Louisiana to determine what relationship drinking Mississippi River water might have on mortality from colon or rectal cancer, found a significant risk for rectal cancer associated with surface water. Rectal and colon cancer deaths (692 and 1,167) from 1969 to 1975 were matched to non-cancer deaths by age at death (+-5 yr), yr of death, sex and race, and within groups of parishes with similar industrial and urban-rural characteristics, each group being defined so as to ensure that it included as nearly as possible equal populations using water from ground and surface sources, based on the 1970 census. Colon cancer did not relate significantly to any water variable, but rectal cancer associated strongly with surface, or Mississippi River, water. The odds ratio for rectal cancer between those who were born and died on ground water was 2.07 with 95% CI: (1.49-2.88). A multi-dimensional emergency contingency table analysis found the association between rectal cancer and surface water significant at the 0.0001 level and not dependent on age, race sex or yr of death. The risk for men was slightly higher than for women, but both sexes showed an increased risk. Chlorination also associated significantly with rectal cancer. Among those who used river water, the risk increased inversely as the distance from the mouth, with greater risk downstream from the many industries which line the river. (Author abstract) (24 Refs)

12. THE RELATIONSHIP BETWEEN WATER QUALITY AND HEALTH IN THE LONDON AREA.

Beresford SA
Dept. Clinical Epidemiology and General Practice, Royal Free Hosp. Sch. Medicine, Pond St., London NW3 2QG, England
Int J Epidemiol; 10(2):103-115 1981

In a retrospective study of the relationship between reuse of water and hazards to health, the mortality experience from different causes, principally cancer, was examined for 29 boroughs and districts in the London area for the period 1968 to 1974. Information concerning the source of water supply to each borough was obtained both for the current situation, and historically back to 1926. Socioeconomic characteristics of the boroughs were extracted from 1971 census data. Differential mortality experiences for each sex were analyzed using the standardized mortality ratio for ages 25 to 74. Most of the causes of death examined were associated with one or more of the socioeconomic characteristics of the boroughs. These socioeconomic characteristics accounted for the statistical associations between water reuse and mortality for each cause studied, except male stomach cancer, where a weak residual association remained. This association disappeared when variation in the size of boroughs was taken in to account. (Author abstract) (34 Refs)

13. A STUDY OF THE GEOGRAPHICAL PATTERN OF CANCER MORTALITY FOR SELECTED SITES BY MEANS OF FACTOR ANALYSIS.

Inaba Y, Yanai H, Takagi H, Yamamoto SI
Dept. Hygiene, Juntendo Univ., Japan
Soc Sci Med [Med Geogr]; 15(1):233-244 1981

Factor analysis of the geographical distribution of cancer mortality in 46 Japanese prefectures during 1958-1971 revealed a significant correlation between the rate of primary industry and skin, prostate, lymphoid tissue, or bladder cancer and leukemia in men. In women, uterine and liver cancer and leukemia correlated positively with natural environmental factors (temperature, precipitation). Lung, intestinal, and oral cancer correlated with population density and appeared to be related to industrialization or urbanization. There was also a significant positive correlation between the rate of primary industry and pancreas and bile duct cancer in women. Esophageal cancer did not correlate with the primary industry rate, the natural environmental factors, or population density. Food consumption in Japan and 24 other countries also was analyzed. Despite the different data sources, similar clustering of cancer sites was noted; ie, prostate, skin, and leukemia for men, skin and leukemia for women, and intestines and lungs for both sexes. (15 Refs)

14. MORTALITY AMONG RUBBER WORKERS. III. CAUSE-SPECIFIC MORTALITY, 1940-1978.

Delzell E, Monson RR
Dept. Epidemiology, Harvard Sch. Public Health, 677 Huntington Ave., Boston, MA, 02115
JOM; 23(10):677-684 1981

This report describes mortality occurring between 1940 and mid-1978 among 29,087 men and women employed in a rubber plant for at least 2 yr. Mortality patterns for the period July 1, 1974, to July 1, 1978, were compared to previously published findings for January 1, 1940, through June 30, 1974. Expected numbers of deaths were based on U.S. general population mortality data. There were excess deaths from bladder cancer and leukemia among white male union members during both follow-up periods. During recent follow-up of white male union members employed for at least 5 yr, there were excesses in deaths from three additional cancers: esophageal cancer (11 observed/4.8 expected), biliary and liver cancer (6 observed/3.3 expected) and lymphoma and multiple myeloma (14 observed/5.8 expected). Evidence from other studies of rubber workers suggests that observed excesses in deaths from bladder cancer and leukemia are related to workplace exposures. The present findings suggest that occupational exposures etiologically relevant to these diseases may not have been reduced in recent yr or that sufficient time has not elapsed for such reductions to result in decreased mortality. Further investigation is required to clarify the contribution of occupational factors to observed excesses in deaths from cancers of the esophagus and the biliary passages and liver and from lymphoma and multiple myeloma. (Author abstract) (26 Refs)

DIETARY AND DIGESTIVE FACTORS IN GI CARCINOGENESIS

15. GALLBLADDER DISEASE: RISK FACTOR FOR COLORECTAL CARCINOMA? (MEETING ABSTRACT).

Allende HD, Ona FV
Department of Medicine, University of Rochester, Rochester, NY
Gastroenterology; 80(5,part2):1099 1981

A study of the relationship between the state of the gallbladder and the risk of colorectal carcinoma is reported. Eight hundred and sixty-four consecutive adult postmortem examinations were reviewed. Data recorded and analyzed were: 1) sex, 2) presence or absence of colorectal cancer, 3) state of the gallbladder, in this study classified as: a) normal, b) cholelithiasis, c) surgically absent. Statistical analysis was carried out by max likelihood and standard Chi-square methods. Gallbladder disease was defined as either cholelithiasis or cholecystectomy. The analysis confirmed the known association between the female sex and gallbladder disease and revealed that after correcting for this association the prevalence of colorectal cancer was higher among cholelithiasis and cholecystectomy cases. The frequency was higher among cholecystectomy than among cholelithiasis cases but this difference was not statistically significant. Previous studies of the possible association between cholecystectomy and colorectal carcinoma have been contradictory, probably because they failed to evaluate the entire spectrum of gallbladder state from health to max disease. It is concluded that the state of the gallbladder modifies the risk of colorectal carcinoma. (no Refs)

16. CHOLELITHIASIS AND CANCER (MEETING ABSTRACT).

Lowenfels AB, Schwartz R, Pitchumoni C
Department of Surgery and Medicine, New York Medical College, Valhalla, NY, 10595
Gastroenterology; 80(5,part2):1218 1981

To investigate the association between gallstones and cancer we have reviewed all autopsy records from patients dying between 1973 and 1979 in two teaching hospitals. There were 547 males and 368 females. The age-adjusted prevalence of gallstones at autopsy was 23% in males and 25% in females, somewhat higher than in previous reports. Twenty-five percent of the entire group had evidence of cancer and there was no overall difference in risk for patients with or without gallstones. However, female patients below age 50 with evidence of gallstones had more cancers than age-matched control patients without gallstones. Analysis of 52 colon cancer cases showed a trend toward an association in females only. Furthermore, the 5 colon cancer patients less than 50 yr had a 13 x greater than expected prevalence of gallstones. The results lend tentative support to the hypothesis that at least in younger female patients there is an association between gallstones and certain diet-related cancers. (no Refs)

17. RELATIONSHIP BETWEEN CHOLECYSTECTOMY AND COLORECTAL CANCER (MEETING ABSTRACT).

Caprilli R, Pietroiusti A, Chierchini P, Giuliano M, Andreoli A, Prantera C
Unita Gastroenterologica II Clinica Medica, Universita di Roma, Rome, Italy
Gastroenterology; 80(5,part2):1120 1981

The records of 773 patients admitted for colorectal cancer to two Rome hospitals during a ten-yr period were retrospectively examined. Diagnosis had been confirmed histologically in all cases. A sex and age matched control admitted to the same hospital during the same calendar period was selected for each case. Fisher's test was used for the analysis of data. Thirty-five (4.5%) patients with carcinoma of the colon and forty-seven (6%) controls had been submitted, 2-31 yr previously, to cholecystectomy but no significant difference was found between the two groups. The difference remained unchanged even when patients with a history of conditions at risk for cholelithiasis were excluded from both groups. Furthermore, the two groups were comparable with respect to longstanding cholecystectomies (more than five yr). The distribution of cancer by subsite was similar in cholecystectomized and non cholecystectomized patients. No gradient of previous cholecystectomy from ascending colon cancer to rectal cancer was found, as reported by others. In conclusion, the results of this study do not indicate that cholecystectomy may be regarded as a risk factor for the development of large bowel cancer and in particular right-sided carcinoma. (no Refs)

18. ASSESSMENT OF THE ROLE OF MUTAGENS AND ENDOGENOUS FACTORS IN LARGE BOWEL CANCER.

Weisburger JH, Spingarn NE, Wang YY, Vuolo LL
American Health Foundation, Valhalla, NY
Cancer Bull; 33(4):124-129 1981

Etiology of large bowel cancer is discussed. The production of abnormal DNA through the direct attack of radiation, chemicals, or viruses, or through improper DNA polymerase activity during DNA synthesis or repair, is only the first step in a long sequence of events terminating in a malignant invasive neoplasm. Rate of cell duplication as controlled by promoters or inhibitors is also important for neoplasm development. Chemical carcinogens, accounting for the majority of human cancers, can be divided into two major groups: genotoxic (direct-acting, procarcinogen, and inorganic carcinogen) and epigenetic (solid-state carcinogen, hormone, immunosuppressor, co-carcinogen, and promoter). Colon cancer incidence and mortality vary as a function of geographic area of residence. The key environmental difference between low-risk and high-risk countries appears related to diet, particulary fat and fiber consumption. In order for colon cancer to occur, both promoters (ie high fat diet) and initiators (ie mutagens produced during frying or broiling of meats and fish) may be required. Variations in these factors and high fiber intake can alter the incidence of colon cancer. (38 Refs)

19. CANCER OF THE COLON AND RECTUM IN THE COLOURED POPULATION OF JOHANNESBURG. RELATIONSHIP TO DIET AND BOWEL HABITS.

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S Afr Med J; 60(15):571-573 1981

In the Colored population of Johannesburg, the incidence of carcinoma of the colon and rectum estimated over an 11-yr period (1970-1980) is 133 and 108/100,000 respectively per yr. This is lower than the incidence reported in Whites and appears to be even lower than that reported in South African and Zimbawean Blacks. A survey of dietary factors in this population showed a diet which was high in protein, low in fats and high in bulk. The frequency of bowel action was higher than in both Whites and Blacks. These factors support Burkitt's hypothesis which states that races with a high-bulk diet have a lower incidence of large-bowel cancer. (Author abstract) (16 Refs)

20. FACTORS ASSOCIATED WITH ADENOCARCINOMAS OF THE LARGE BOWEL IN PUERTO RICO.

Martinez I, Torres R, Frias Z, Colon JR, Fernandez N
Cancer Control Program, Dept. Health, Puerto Rico
Rev Latinoam Oncol Clin; 13(1):13-20 1981

A case-control study of 461 patients with adenocarcinoma of the colon seen during the period 1973-1975 and 461 sex- and age-matched controls was conducted. Subjects or relatives (102 pairs) were questioned on long-term dietary and personal habits, and familial aggregation of cancer. Of the 461 adenocarcinomas, 232 were in the colon and 229 were in the rectum and rectosigmoid junction (1.2:1 male-female ratio). Highest number of patients were 65-74 yr old. Twenty-two percent of patients were professionals vs 18.5% of controls. Significantly more patients (29.1%) than controls (16.5%) were heavy cigarette smokers. Patients reported significantly greater frequency of consumption of meats (34.7% high frequency vs 24.3% in controls), cereals (26.7% vs 18.7%), fats (49.2% vs 36.7%), total residue (36.4% vs 29.5%), and fiber (51.4% vs 42.3%). Patients also had more previous nonmalignant chronic disease of the large bowel (diverticulosis, intestinal polyposis, ulcerative colitis, other types of colitis, chronic constipation, diarrhea, and hemorrhoids), higher grade of constipation, and more direct relatives with cancer (for cancer of the large bowel, 22 relatives among patients vs 9 among controls). Recall bias may be expected in this type of study. (25 Refs)

21. CARCINOGENESIS OF GASTRIC CANCER WITH SPECIAL REFERENCE TO ETIOLOGICAL ASPECTS.

Schmahl D
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Zentralbl Chir; 106(15):997-1004 1981

The article discusses possible etiological factors for the carcinogenesis of stomach tumors. Apart from genetic factors, stomach carcinogenesis may be attributed to the exposure of the stomach to carcinogenic substances taken in with the food, such as pyrolysis products of certain amino acids, N-nitroso compounds or disturbances of the physiological function of the stomach, for example pathological reflux after stomach operations. The frequency of stomach cancer could not be related to occupational exposure. Geographic pathology has shown that people coming from high risk areas (eg Japan) adapt to the risk pattern of the host country when they emigrate (eg to the United States, where there is only a low risk for stomach cancer). Therefore, it is assumed that several factors play a role in the etiology of stomach cancer. (Author abstract) (16 Refs) (In GER)

OTHER ETIOLOGIC FACTORS IN GI CARCINOGENESIS

22. DISTRIBUTION OF MALIGNANT POLYPS IN THE COLON (MEETING ABSTRACT).

Appel MF
Department of General and Thoracic Surgery, Kelsey-Seybold Clinic, St. Luke's Episcopal Hospital, Houston, TX
Gastroentest Endosc; 27(2):119 1981

The purpose of this investigation was to ascertain the spacial distribution of malignant polyps in the colon and to compare this with the distribution of non-malignant neoplastic polyps. In this study, a consecutive and unselected series of 1,226 polyps was analyzed. The classes of neoplastic polyps characterized were pure adenomas, villoglandular, villous adenoma, and carcinoma. The location of all polyps in general corresponds to the usual distribution and indicates that 52% of the polyps were in the sigmoid colon, 20% were in the descending colon, 16% in the transverse colon, and 13% in the ascending colon and cecum. Of the polyps with carcinoma in them, however, 83% of these were located in the sigmoid colon, 12% were in the descending colon, 2% were in the transverse colon, and 2% were in the ascending colon and cecum. The conclusion is made that the vast majority of polyps with malignancy in them (95%) is located in the left side of the colon, from the splenic flexure down. A relatively small number (4%) of polyps with malignancy in them exists in the right colon and in the transverse colon. The study does suggest that periodic examination of the left colon is important, and that all polyps found in this area be removed. (no Refs)

23. CARCINOMA OF THE LARGE INTESTINE WITH SCHISTOSOMIASIS --ANALYSIS OF 279 CASES.

Zhao E, Weng Y
Dept. Surgery, Hangzhou Cancer Hosp., Hangzhou, People's Republic of China
Zhonghua Zhongliu Zazhi; 3(1):67-69 1981

Clinical findings are described for 279 cases of large intestinal carcinoma with schistosomiasis (males/females ratio 1.85/1; aged 20-69 yr) and compared to those of 653 cases without schistosomiasis (males/females ratio 1.6/1; aged 16-69 yr) seen between 1963 and 1977. Most of the carcinomas were located in the rectum and sigmoid colon. No significant difference was observed in the histopathological classification of the two groups. However, Dukes' staging and lymph node metastatic status revealed considerably less lymph node metastasis and earlier Dukes' stage in the complicated than in the non-complicated group. The 5-yr survival rates in both groups were the same (approx 53%) though the operative mortality in the complicated group was much higher (3.42% vs 0.80%). The resection rates of the complicated and non-complicated groups were 59.34% and 65.49% respectively. It is postulated that schistosomiasis may lead to the development of carcinoma in the large intestine. (3 Refs) (In CHI)

24. ESOPHAGEAL CANCER AMONG BLACK MEN IN WASHINGTON, D.C. I. ALCOHOL, TOBACCO, AND OTHER RISK FACTORS.

Pottern LM, Morris LE, Blot WJ, Ziegler RG, Fraumeni JF
Environmental Epidemiology Branch, Div. Cancer Cause and Prevention, NCI, NIH, Public Health Service, U.S. Dept. Health and Human Services, Bethesda, MD, 20205
JNCI; 67(4):777-783 1981

A case-control study involving interviews with the next of kin or close friends of 120 black males who recently died of esophageal cancer and 250 similarly aged black males who died of other causes was undertaken to discover reasons for the exceptionally high mortality from this cancer in Washington, DC. The age-adjusted annual death rate in Washington, DC, for nonwhite males, 1970-75, was 28.6/100,000 far higher than the national rate of 12.4/100,000 and the rates in other metropolitan areas of the country. The major factor responsible for the excess was alcoholic beverage consumption, with an estimated 81% of the esophageal cancers attributed to its use; high use of alcoholic beverages was also found among the controls. The relative risk (RR) of esophageal cancer associated with use of alcoholic beverages was 6.4 (95% confidence interval = 2.5, 16.4). The RR increased with amount of ethanol consumed and was highest among drinkers of hard liquor, although the risk was also elevated among consumers of wine and/or beer only. The RR associated with cigarette smoking was 1.9 (1.0, 3.5) when controls with smoking-related causes of death were excluded but declined to 1.5 (0.7, 3.0) when adjusted for ethanol consumption. Significant differences of approx twofold were found between low and high levels of (a) consumption of fresh or frozen meat and fish, fruits and vegetables, and dairy products and eggs and (b) relative wt (wt/ht2). The inverse trends with these general measures of nutritional status were not explained by alcoholic beverage consumption of socioeconomic status as measured by educational level. (Author abstract) (23 Refs)

25. A NEW LOOK AT THE CANCER RISK IN ULCERATIVE COLITIS (MEETING ABSTRACT).

Gyde S, Prior P, Waterhouse JA, Allan RN
Gastroenterology Unit, The General Hospital, Birmingham, England
Gut; 22(5):A418 1981

The magnitude and pattern of risk of colorectal cancer in ulcerative colitis is uncertain, the apparent risk varying greatly from one reported series to another. In this analysis several models have been used to show how selection factors, operating in most reported series, may alter the apparent cancer risk and the pattern of risk over time. These models have been applied to a hospital series of 676 patients under long-term review with ulcerative colitis. The number of colorectal and hepatobiliary cancers observed in the series was significantly in excess of that expected in a comparable general population. The colorectal cancer risk varied from six to 17 x that in the general population according to which model was used for analysis. This variation helps to explain the widely differing estimates of colorectal cancers in published series. The model which seems to most closely resemble the natural history of the disease suggests that the risk of developing colorectal cancer increases in the first 15 yr after onset of ulcerative colitis and thereafter becomes a constant increased risk. This pattern suggests that cancer may be initiated and colitis induced by a common etiological agent at or near the onset of colitic symptoms. (no Refs)

26. FAMILIAL INCIDENCE OF COLORECTAL CANCER (MEETING ABSTRACT).

Duncan JL, Kyle J
Gastrointestinal Research Unit, Royal Infirmary, Aberdeen, Scotland
Gut; 22(5):A435 1981

A prospective study of the familial incidence of cancer has been performed on 50 consecutive patients treated for adenocarcinoma of the colon and rectum. All diagnoses were confirmed histologically and the presence or absence of adjacent polyps was noted. Each patient was questioned about all first-degree relatives, particularly in regard to intestinal cancer. Confirmation was obtained from pathology reports or close relatives. The control group consisted of 50 patients, matched for age and sex, and who did not have cancer. Nine out of the 50 patients had a parent, sibling, or child with colorectal cancer (18%). In five out of the nine families the mother was the other affected member. In the control group only two patients had an affected relative (4%). The difference is highly significant. The familial incidence was, comparable with the 16% incidence noted in Nebraska, but the 'cancer families' with more than two affected members were not encountered in the present series. There was no difference in the frequency of polyps in the group of patients who had affected relatives (22%) compared with the group whose close relatives to date are free from colorectal cancer (24%). The implications for screening programs are discussed. (no Refs)

INDUCTION OF GI CARCINOGENESIS IN ANIMALS

27. COMPARATIVE STUDIES ON THE PRODUCTION OF STOMACH TUMORS FOLLOWING THE INTUBATION OF SEVERAL DOSES OF N-METHYL-N'-NITRO-N-NITROSOGUANIDINE IN GERM-FREE AND CONVENTIONAL NEWBORN RATS.

Sumi Y, Miyakawa M
Lab. Germfree Life Res., Nagoya Univ. Sch. Medicine, 65 Tsuruami-cho, Showa-ku, Nagoya 466, Japan
Gan; 72(5):700-704 1981

The present work was undertaken to investigate the possible role of microflora in gastric tumorigenesis by the comparison of tumor production between germ-free and conventional male Wistar rats given the same amount of N-methyl-N'-nitro-N-nitrosoguanidine into the stomach by catheter during the newborn period. Only 29% of germ-free rats treated with 450 ug/animal that were killed 300 days after the first intubation had tumors in the stomach, whereas 93% of conventional similarly treated rats had such tumors at the same period, suggesting that the microflora might exert a promoting influence upon stomach tumor production. (Author abstract) (27 Refs)

28. PARTIAL COLECTOMY PROMOTES EXPERIMENTAL CARCINOGENESIS ONLY AT THE SITE OF INTESTINAL ANASTOMOSIS (MEETING ABSTRACT).

Williamson RC, Davies PW, Bristol JB, Wells M
University Department of Surgery, Royal Infirmary, Bristol, England
Gut; 22(5):A440 1981

The possibility that metachronous colorectal cancers arise in mucosa rendered hyperplastic by partial intestinal resection was tested in male Sprague-Dawley rats weighing 159 +/-14 g (standard deviation). Rats received mid-colonic transection, right or left hemicolectomy, cecal resection, or no operation (controls). Each operation was performed either before or one wk after a course of five weekly sc injections of azoxymethane (10 mg/kg/wk) or water. The timing of operation did not affect ultimate tumor yields. Although cecal resection and right hemicolectomy both increased ileal wet wt by 22-40%, there was no evidence of adaptive growth in the colon after partial colectomy. A total of 217 large-bowel tumors were distributed as follows: proximal colon 16.5%, colonic anastomosis 23.5%, distal colon 40%, rectum 20%. Consistent with this leftsided predominance, left hemicolectomy reduced the number of tumors by 52-58% compared with transection or controls. Cecal resection had no effect. A twofold increase in distal tumors after transection and right hemicolectomy reflected the many anastomotic tumors found after each operation. Moreover, one rat receiving vehicle (not carcinogen) developed an invasive mucinous adenocarcinoma at the colorectal anastomosis after left hemicolectomy. Ileocolic and colorectal anastomoses are favored sites for tumor development after partial colectomy. The lack of adaptive hyperplasia may explain unaltered carcinogenesis in the remaining colon. (no Refs)

29. COMPARISON OF THE CARCINOGENICITY OF METHYLAZOXYMETHANOL-BETA-D-GLUCOSIDURONIC ACID IN CONVENTIONAL AND GERMFREE SPRAGUE-DAWLEY RATS.

Laqueur GL, Matsumoto H, Yamamoto RS
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JNCI; 67(5):1053-1055 1981

Methylazoxymethanol-beta-D-glucosiduronic acid (MAM-GlcUA) was administered to young adult male Sprague-Dawley rats by oral and ip routes. Most neoplasms developed in rats that had received the compound po. The most prevalent site for the neoplasms was the intestinal tract, predominantly the colon. Comparatively fewer tumors occurred in the liver and kidneys. Germfree rats did not develop tumors when MAM-GlcUA was administered either po or ip. (Author abstract) (9 Refs)

30. EXPERIMENTAL RESEARCH ON THE CARCINOGENIC ACTIVITY OF EPICHLOROHYDRIN BY ORAL ADMINISTRATION IN MALE WISTAR RATS.

Kawabata A
Second Dept. Internal Medicine, Nara Medical Univ., Nara, Japan
Nara Igaku Zasshi; 32(3):270-280 1981

Carcinogenic activity of epichlorohydrin (E) administered in drinking water ad libitum to 72 male Wistar rats for 81 wk is reported. The rats were divided into four groups; Group 1 were given drinking water without E, Group 2 were given 375 ppm E in drinking water, Group 3 were given 750 ppm E in drinking water, and Group 4 were given 1,500 ppm E in drinking water. Following wk 81 of the experiment, various hematological analyses were performed in rats from each group, and the rats were sacrificed in order to histologically examine any resulting tumors. In Group 2 were observed macroscopically 5.6 +-8.4 tumor foci in the forestomachs, and 7/9 rats had hyperplasia of the gastric epithelium. In Group 3 were seen 9.9 +-12.8 tumor foci in the forestomachs; hyperplasia was noticed in 9/10 rats, papilloma in 1/10, and squamous cell carcinoma in 1/10. In Group 4 were seen 32.8 +-24.0 tumor foci in the forestomachs; hyperplasia was observed in 12/12 rats, papilloma in 7/12, and squamous cell carcinoma in 2/12. No tumors were observed in Group 1. Also, squamous cell carcinoma of the oral cavity was observed in 3/12 rats of Group 4, mesotheliomas were observed in 2/10 rats of Group 1, 2/9 in Group 2, 4/10 in Group 3, and 3/12 in Group 4. The results suggested that E had a direct carcinogenic effect on rats. (26 Refs) (In JPN)

31. CANCER INDUCTION IN MICE WITH ACETALDEHYDE METHYLFORMYLHYDRAZONE OF THE FALSE MOREL MUSHROOM.

Toth B, Smith JW, Patil KD
Eppley Inst. Res. in Cancer and Allied Diseases, Univ. Nebraska Medical Center, Omaha, NE, 68105
JNCI; 67(4):881-887 1981

Acetaldehyde methylformylhydrazone (AMFH), which occurs up to 0.3% in one of the edible false morel mushrooms, Gyromitra esculenta, was administered to noninbred Swiss mice in propylene glycol in 52 weekly intragastric instillations as 100 ug/g body wt. The treatment induced tumors of the lungs, preputial glands, forestomach, and clitoral glands. The tumor incidences in these four tissues in treated females were 70, 0, 16, and 12%, respectively, whereas in the treated males they were 40, 90, 0, and 0%. The corresponding tumor incidences in the solvent control females were 26, 0, 0, and 0%, whereas in the solvent control males they were 22, 0, 0, and 9%, respectively. Histopathologically, the neoplasms were classified as adenomas and adenocarcinomas of the lungs; squamous cell papillomas and carcinomas, adenocarcinomas, undifferentiated carcinomas, angiosarcomas, and fibrosarcomas of the preputial glands; squamous cell papillomas and carcinomas of the forestomach; and squamous cell papillomas and carcinomas and keratoacanthomas of the clitoral glands. The study thus proves for the first time the tumorigenicity of AMFH. In view of these and earlier findings, the human population should abstain from consumption of Gyromitra esculenta. (Author abstract) (21 Refs)

MECHANISMS AND MODIFICATIONS OF GI CARCINOGENESIS

32. EFFECT OF ANTIBIOTICS ON INCIDENCE OF RAT INTESTINAL TUMORS INDUCED BY 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE.

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JNCI; 67(4):877-880 1981

The intestinal microflora has been shown to influence the induction of chemical carcinogens responsible for intestinal tumors in animal models. For further exploration of this issue, male inbred F344 rats were administered a chemical carcinogen, 1,2-dimethylhydrazine dihydrochloride (DMH), for 20 wk, along with oral antibiotics, either tetracycline or erythromycin, to suppress the intestinal flora. Colon cancer incidence was lower in animals receiving antibiotics; 22% of the erythromycin-treated rats and 20% of the tetracycline-treated rats had colon tumors compared to untreated controls with a 74% tumor incidence (p less than 0.002). Tumors in the small intestine also decreased from an incidence of 48% in the control animals to an incidence of 27 and 7%, respectively, for the erythromycin- and tetracycline-treated rats. These findings suggested that the metabolic activity of the intestinal flora is related to cancer induction by DMH. (Author abstract) (23 Refs)

33. DNA METHYLATION BY N-NITROSOMETHYLBENZYLAMINE IN TARGET AND NON-TARGET TISSUES OF NMRI MICE.

Kleihues P, Veit C, Wiessler M, Hodgson RM
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Carcinogenesis; 2(9):897-899 1981

Correlations between initial DNA methylation and preferential sites of tumor induction were examined in adult female NMRI mice given a single ip injection of 14C-labeled N-nitrosomethylbenzylamine (MBN: 2.5/kg). Weekly applications of such a dose administered by the same route induced forestomach carcinomas and lung adenomas in all experimental animals. Lung and forestomach 7-methylguanine and O(6)-methylguanine levels were considerably lower than hepatic levels, but they were higher than the levels in nontarget tissues. The initial extent of DNA methylation in the esophagus was only 21% abbreviation) less than that in the forestomach. Since po MBN results in tumors in both tissues, the results suggested that a different level of DNA modification is required for tumor induction in these tissues. The reason for the resistance of liver cells to methylating carcinogens remains unclear. (7 Refs)

34. METAL INTERACTIONS IN CARCINOGENESIS: ENHANCEMENT, INHIBITION.

Nordberg GF, Andersen O
Dept. Environmental Hygiene, Umea Univ., Umea, Sweden
Environ Health Perspect; 40:65-81 1981

The roles of metals in enhancing or inhibiting carcinogenesis are reviewed. Conclusive evidence of the carcinogenicity of arsenic has not yet been found, although some studies suggest it. Arsenic may act as a cocarcinogen. Selenium seems to be weakly mutagenic in bacteria and some mammalian cell cultures. Antitumor properties have been reported in experimental animals. Zinc is necessary as a trace element in the diet and may have anticarcinogenic effects. Nickel is strongly carcinogenic in experimental animals and humans. Its effects may be counteracted by manganese. Lead has not been confirmed as a carcinogen, but its presence in the environment warrants high priority research particularly on its effects in combination with other compounds. Chromium has been related to lung, and possibly stomach, cancer in man. Cadmium contributes to prostatic cancer and Leydig cell tumors. These effects can apparently be counteracted by zinc treatments. Carcinogenesis by benzo[a]pyrene, nitrosamines, and asbestos appear to be promoted by some metallic dusts. Further studies in vitro and in appropriate animal systems are urged. (155 Refs)

35. THE ORGAN CULTURE OF RAT ESOPHAGEAL MUCOSAL EPITHELIUM AND ITS RESPONSE TO N'-NITROSONORNICOTINE (MEETING ABSTRACT).

Reiss B, Hecht SS, Williams GM
Naylor Dana Institute for Disease Prevention, American Health Foundation, Valhalla, NY, 10595
In Vitro; 17(3):223 1981

Using techniques similar to those beneficial for the prolonged organ culture of rodent colon, we have maintained rodent esophagus for up to 35 days. During this interval, the normal architecture and histology of the mucosal epithelium were preserved, and normal cell proliferation and keratinization were retained. Kinetic studies of cells labelled during DNA synthesis demonstrated a continuation of epithelial cell maturation and migration for at least 4 wk. Exposure to the model esophageal carcinogen, N'-nitrosonornicotine (NNN; 10(-2) M) for 48 hr in culture suppressed DNA synthesis of conventional rat esophageal mucosa at 2 days; higher incorporation than controls occurred at 1, 2 and 3 wk. Exposure to 14C-NNN for 48 hr resulted in the formation of 4-oxo-4-(3-pyridyl)butyric acid from 2'-hydroxylation and 4-hydroxy-4-(3-pyridyl)butyric acid from 5'-hydroxylation of NNN. The levels of these metabolites indicated that, unlike the hepatic metabolism of NNN, the extent of 2'-hydroxylation in the esophagus exceeds that of 5'-hydroxylation. These results may provide the metabolic basis for the organo-selectivity of NNN. Fragments of organ-cultured esophagus implanted into mammary fat pads of syngeneic animals have been maintained for up to 6 mo. Fragments exposed to NNN for 48 hr and then implanted developed a hyperplastic mucosal epithelium after 2 mo in the host. This potentially preneoplastic change was not observed in controls. (1 Ref)

36. EFFECTS OF CHRONIC ADMINISTRATION OF NEOMYCIN ON INTESTINAL CARCINOGENESIS IN THE AZOXYMETHANE (AOM)-TREATED-RAT MODEL (MEETING ABSTRACT).

Hamilton SR, Stephens RB, O'Ceallaigh D, Natuzzi E, Dick E, Boitnott JK, Baker RR, Yardley JH
Depts. of Pathology and Surgery, The Johns Hopkins Hospital, Baltimore, MD, 21205
Gastroenterology; 80(5,part2):1167 1981

Chronic oral administration of neomycin has been reported to promote experimental colon carcinogenesis. Effects of neomycin were studied in male Sprague-Dawley rats given 10 weekly sc injections of 14.5 mg/kg AOM, a potent bowel carcinogen, and killed 24 wk after first dose. Neomycin 0.5 mg/ml in distilled water was given as sole drinking fluid during the 10-wk course of AOM (WITH-AOM group), during the 14 wk after AOM was completed (POST-AOM), or for the full 24 wk (THRU-OUT). The CONTROL group received sc AOM and oral distilled water. Preliminary fecal bacteriologic studies showed that neomycin produced transient reduction in aerobic bacteria only. The two groups receiving neomycin after the course of AOM was completed (POST-AOM and THRU-OUT) showed a striking increase in both small and large bowel tumors. In contrast, administration of neomycin only during the course of AOM (WITH-AOM) increased small bowel tumors but caused no statistically significant increase in total colon tumors or actually decreased proximal colon tumors. Our findings confirm the promotion of experimental bowel carcinogenesis by chronic oral neomycin. Furthermore, they suggest that promotion in the colon occurred in mucosa rendered tumor-prone by previously administered AOM. Finally, the variability of effects, depending upon times of administration and portion of bowel studied, suggests that neomycin, which produced transient reduction of aerobic bacteria only, may effect carcinogenesis by mechanisms other than modification of fecal flora. (no Refs)

37. TRANSFORMATION OF EPITHELIAL CELLS FROM CARCINOGEN-TREATED RAT ESOPHAGUS (MEETING ABSTRACT).

Stoner GD, Babcock MS
Medical College of Ohio, Toledo, OH, 43614
In Vitro; 17(3):236 1981

In this report, we describe the development of an in vitro model for the study of carcinogen induced esophageal cancer. Primary explant cultures of rat esophagus were treated with the potent esophageal carcinogen, N-nitrosomethylbenzylamine (MBN) at concentrations of 10, 5, 2.5 and 1 ug per ml on days 1 and 7 after initiation of the cultures. After incubation for 2-3 mo, epithelial cells in cultures treated with 10, 5 or 2.5 ug per ml could be subcultured and cell lines developed. Attempts to subculture epithelial cells from explants treated with either 1 ug MBN per ml or with dimethylsulfoxide (solvent control) were unsuccessful. Electron microscopy revealed that the subcultured cells contain morphological markers of epithelial cells: numerous tonofilaments and junctional complexes. By immunofluorescence, the cells reacted positively with antibodies prepared to mouse skin keratins. In early passage, the growth of the cells was stimulated by the addition of epidermal growth factor to the medium. Some of the cell lines exhibited characteristics of neoplastic cells: they are aneuploid, form colonies from single cells in soft agar, and produce squamous cell carcinomas after transplantation into syngeneic newborn rats or athymic, nude mice. (no Refs)

38. MECHANISM OF FIBRE PROPHYLAXIS OF CHEMICALLY INDUCED COLONIC CARCINOMA IN THE RAT (MEETING ABSTRACT).

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Department of Surgery, University Hospital of Wales, Heath Park, Cardiff CF4 4XN, England
Eur Surg Res; 13(1):96 1981

The prophylactic effect of fiber on colonic carcinogenesis may be due to a reduction in energy intake rather than an effect on stool bulk and transit time. To test this hypothesis colon cancer was induced in rats whose diet was varied for energy intake as well as fiber intake. Sixty-two weanling rats were divided into four groups, matched for wt and rate of growth. All animals were given sc injections of dimethylhydrazine dihydrochloride (20 mg/kg at 10-day intervals for 150 days). The animals were housed and fed as follows until sacrificed at 170 days: group 1: normal diet ad lib, caged in fours; group 2: high fiber diet ad lib, caged in fours; group 3: high fiber diet ad lib, caged singly; group 4: normal diet restricted to the same energy, intake as group 3, caged singly. Adult mean wt with cancer incidences (in parentheses) were: group 1: 421 g (14/16); group 2: 391 g (14/16); group 3: 369 g (8/15); group 4: 358 g (10/15). There were no significant differences in cancer incidences between any of the groups taken individually and simply feeding fiber was not seen to offer any protection. Groups 1 and 2 combined had a significantly higher incidence of cancer than the smaller animals in groups 3 and 4 combined, which favors the hypothesis that any effect that fiber may have is related to cal restriction rather than to its mechanical effects in the bowel. (no Refs)

39. THE EFFECTS OF SODIUM BUTYRATE ON EPIDERMAL GROWTH FACTOR BINDING TO HUMAN COLORECTAL CANCER CELLS (MEETING ABSTRACT).

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Gastroenterology; 80(5,part2):1267 1981

Epidermal Growth Factor (EGF), a 6000 mol wt protein hormone produced by salivary and Brunner's glands, has been shown to have a mitogenic effect in normal intestine. Work in our laboratory has demonstrated that EGF stimulates the growth of human adenocarcinoma cells in culture as well as binding to a 180,000 mol wt cell surface receptor. Sodium butyrate (NaBt) has been reported to induce differentiation in some cancer cell systems. In this study a human rectal carcinoma cell line (HRT-18) and a human colon adenocarcinoma cell line (HT-29), whose growth is stimulated by EGF, were grown in the presence of NaBt to assess alterations in growth, tumorigenicity, EGF receptor numbers and characteristics. NaBt treated cells in both cell lines exhibited longer doubling times, lower saturation densities, and an inability to demonstrate anchorage independent growth when compared with control nontreated cells. A significant increase in receptor numbers was noted when expressed as binding per well or binding per mg protein. HRT-18 demonstrated a two-fold increase while HT-29 demonstrated a 1.3 fold increase after incubation with 2mM NaBt. This increase appears to require protein synthesis. Gel filtration and lectin affinity chromatography suggested that the EGF-receptor complex is a glycoprotein. In summary, NaBt can cause changes in cell growth in human colon cancer cells, suggesting lower tumorigenicity, while at the same time causing quantitative changes in EGF receptors. (no Refs)

40. CANCER INDUCTION AFTER PYLOROPLASTY IN RATS TREATED WITH N-METHYL-N'-NITRO-N-NITROSOGUANIDINE (MNNG) (MEETING ABSTRACT).

Salmon RJ, Deschner EE, Okamura T, DeCosse JJ, Sherlock P
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Gastroenterology; 80(5,part2):1268 1981

Since vagotomy and pyloroplasty are more widely used at the present time and vagotomy by itself has been described in animal models as increasing the number of gastric cancers, the effect of duodenal reflux induced by pyloroplasty on cancer induction was investigated in this study. Wistar male rats (19) received MNNG for 12 wk at a dose level of 83 mg/l in the drinking water to initiate glandular adenocarcinoma of the stomach while 3 rats serving as controls received tap water. At the end of 12 wk a pyloroplasty was carried out in 9 rats having received MNNG (Group I) and in 3 controls (Group III). The remaining 10 MNNG treated (Group II) and 5 controls (Group IV) were not operated. All rats were observed for a total period of 38 wk before being sacrificed. No difference in the incidence of MNNG-induced antral adenocarcinomas was found between the Groups I and II. However, in this model a high incidence of duodenal tumors was observed: the unoperated MNNG treated (Group II) animals showed in situ changes in the duodenum while the pyloroplasty group showed 5 massive invasive adenocarcinomas (Group I). It is concluded that, in this model, pyloroplasty alone does not increase the risk for gastric cancer but increases the risk for duodenal tumors. Pyloroplasty accelerates the gastric evacuation rate which in turn results in insult to the duodenal mucosa. Such a condition may require a higher proliferative rate in the duodenum and increase subsequent formation of malignant tumors. (no Refs)

41. PLASMA ZINC AND VITAMIN A IN HUMAN SQUAMOUS ESOPHAGEAL CANCER (MEETING ABSTRACT).

Mellow MH, Layne EA, Lipman TO, Kaushik M, Hostetler C, Smith JC
Veterans Administration Medical Center, Washington, DC, 20422
Gastroenterology; 80(5,part2):1229 1981

Experimental zinc deficiency in animals promotes esophageal tumor induction with chemical carcinogens. Retinoid administration has suppressed tumor progression in animals. Decreased plasma zinc and vitamin A have been noted in several human squamous cancers. We measured plasma zinc and vitamin A in alcoholic patients with newly diagnosed squamous esophageal cancer and compared these to three age-matched control groups: alcoholics without cancer; non-alcoholics with non-squamous cancer; non-alcoholics without cancer. Patients with factors thought to reduce plasma zinc or vitamin A were excluded: severe liver disease, severe protein energy malnutrition, infection, other acute illness. Conclusions: 1) Alcoholic patients with esophageal cancer have significantly decreased mean plasma zinc values compared to non-alcoholics without cancer. This is unlikely due to alcohol ingestion per se since 6 of 12 alcoholics without cancer had normal zinc values. This is also not due to the presence of a cancer since the non-alcoholics with cancer had normal zinc. 2) Patients with esophageal cancer as well as non-esophageal cancers had low mean plasma vitamin A. Our findings suggest a true deficiency of zinc and/or vitamin A nutrition in patients with esophageal cancer, which may have preceded the onset of illness. Zinc and/or vitamin A deficiency may contribute to the development of esophageal cancer. (no Refs)

42. COLORECTAL CANCER - TUBERCULOSIS CONNECTION.

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Med J Aust; 1(12):637-638 1981

Tuberculosis is common in countries with a low incidence of colorectal cancer. A survey was made to determine whether there was any difference in mortality from colorectal cancer in Australia between matched groups with, and without, tuberculous disease. Four hundred consecutively deceased tuberculous patients were compared with a similar number proved not to have contracted any tuberculous infection, and were matched by age, sex, yr of death, and socioeconomic ethnic status. There was a statistical significance (p less than 0.01) for colorectal and other gastrointestinal cancers, but not for other cancers. In the non-tuberculous group, there were 21 deaths from colorectal and 24 deaths from other gastrointestinal cancers compared to 7 deaths from colorectal and 7 from other gastrointestinal cancers in tuberculous patients. Increased immunity against the tubercle bacillus may have played a part in these findings. (Author abstract) (5 Refs)

43. HIGH DIETARY CELLULOSE: PROTECTION AGAINST LARGE BOWEL CARCINOMA (MEETING ABSTRACT).

Prizont R, Piatt K

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Gastroenterology; 80(5,part2):1256 1981

The effect of high cellulose diet in experimental carcinogenesis, was investigated in Wistar rats injected ip with 10 doses of 1,2 dimethylhydrazine (DMH). Ten experimental animals (ER) were fed a regular diet of casein (20%), sucrose (50%), fat (5%) and cellulose fiber (5%). A second group (EHF) received a similar diet modified by an increase of cellulose (to 15%) and a concomitant 10% decrease of sucrose. Two groups of 6 rats each were injected with buffer and used as animal controls on a regular or high fiber diet. When food consumption was measured, ER animals averaged 20.5 +/-0.3 g/day and EHF rats, 22.7 +/-0.3 g/day. In the same period of time, ER animals had significantly (p less than 0.005) lower fecal outputs than did EHF rats. Rats were sacrificed 7 mo after initial DMH injection. Conversely, 17 intestinal tumors were found in ER animals, which was significantly higher than the 4 recovered from EHF rats. Histological examination revealed that 15 of the 17 ER tumors were malignant (14 adenocarcinomas and 1 signet ring carcinoma). Only 2 of the EHF tumors were adenocarcinomas. The small intestine of ER rats contained 9 tumors (8 adenocarcinomas). The same area in EHF animals yielded 4 tumors (2 malignant). The large intestine of ER rats contained 8 neoplasms (7 malignant), but no benign or malignant tumors were found in the EHF large bowels. This study indicates that DMH injected rats fed a high cellulose diet develop significantly fewer intestine tumors. (1 Ref)

44. FAILURE OF DIETARY CELLULOSE FIBER TO PREVENT COLON TUMORS IN DIMETHYLHYDRAZINE (DMH)-TREATED RATS ON HIGH CHOLESTEROL DIETS (MEETING ABSTRACT).

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Gastroenterology; 80(5,part2):1301 1981

A prior study has suggested that dietary fiber (cellulose) may decrease colon carcinogenesis in the DMH-induced rat model. We have evaluated the effect of dietary cellulose fiber on DMH-induced colon tumors in rats fed high cholesterol diets (a suspected co-carcinogen with DMH). Synthetic diets containing excess cholesterol and variable fiber content were fed to male Sprague-Dawley rats: Group I (0% fiber), Group II (5% fiber), and Group III (20% fiber). Half of each group received sc injections of DMH for 20 wk. Control rats received saline. All animals were sacrificed 1 wk after the last injection and blood obtained for cholesterol determination. Rat colons were inspected grossly and microscopically for invasive adenocarcinoma. Saline control animals were tumor free. No difference in either tumor incidence or number of tumors per affected rat colon was observed. Furthermore, the presence of dietary fiber did not alter serum cholesterol level supporting prior observations that cellulose fiber does not affect cholesterol metabolism. These findings suggest excess dietary cholesterol may diminish the protective effect of dietary fiber on DMH-induced colon tumors, possibly through an intraluminal mechanism. (1 Ref)

45. ENHANCING EFFECT OF HYDROGEN PEROXIDE UPON DUODENAL AND UPPER JEJUNAL CARCINOGENESIS IN RATS.

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Gan; 72(5):811-812 1981

A study of the incidence of intestinal carcinomas induced in rats by the oral administration of hydrogen peroxide (HP) and methylazoxymethanol acetate (MAMA) injections is reported. In Group A, 8/8 rats developed a total of 21 adenocarcinomas (AC) of the duodenum and 7 jejunal AC following oral administration of 1.5% HP for 21 wk with three ip injections of MAMA given at 2 wk interval during the HP administration. In Group B, 2/8 rats developed AC of the jejunum, and 1/8 developed colonic carcinoma following oral administration of HP for 8 wk including intervals between MAMA injections as in Group A. In Group B, however, HP drinking was discontinued following the injections. In Group C, hyperplastic epithelia of the duodenum and upper jejunum were observed in three rats on HP administration for 25 wk. No neoplastic changes were found in this group or in Group D of three untreated control rats. It is suggested that hyperplastic conditions preinduced by HP prior to the injection of MAMA may have contributed to the development of duodenal and upper jejunal AC. (2 Refs)

46. GLYCOPROTEIN DEGRADING GLYCOSIDASES IN EXPERIMENTAL CANCER OF THE COLON (MEETING ABSTRACT).

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Gastroenterology; 80(5,part2):1255 1981

In this study, we have investigated the non-blood group degrading beta-Galactosidase (beta-Galase) and beta-N-Acetylglucosaminidase (beta-Glnase) in experimentally induced colonic cancer. Ten Wistar rats (ER) were injected for 10 wk with 25 mg/kg of 1,2 dimethylhydrazine (DMH) and fed a diet containing casein (20%), sucrose (50%), fat (5%) and cellulose fiber (5%). Another group of 10 rats (EHF) were similarly injected with DMH but the aforementioned diet was modified by both an increase in cellulose (to 15%) and a decrease in sucrose (to 40%). Two groups of rats, 6 each, were injected with buffer and served as controls for regular (CR) or high fiber (CHF) diets. Feces were collected, homogenized in saline and centrifuged to sediment the bacteria. Bacteria free supernatants were then used for analytical assays against p-nitro-phenylglycosides. When control and experimental animals were compared by diet (CHF vs EHF, CR vs ER), no significant differences in the enzyme levels were found. When animals were sacrificed 7 mo post-initial injection, significantly more tumors were recovered from large and small bowels of ER animals than were recovered from small bowels of EHF rats. This study suggests that high cellulose diets significantly decrease production of fecal non-blood group degrading glycosidases. (2 Refs)

47. ACTIVATION OF N-2-ACETYLAMINOFLUORENE BY TARGET AND NONTARGET SYRIAN GOLDEN HAMSTER CELLS (MEETING ABSTRACT).

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In Vitro; 17(3):222 1981

The ability to metabolize and activate N-2 acetylaminofluorene (AAF) of Syrian golden hamster kidney, bladder, small intestine, lung and liver cells was compared with that of hamster embryo fibroblasts. At varying times after isolation, cells were exposed to 5 ug [14C]-AAF for 3, 6 or 24 hr. The level of AAF remaining and the amount bound to cellular components were determined. Within 3 hr, hepatocytes and intestinal cells had metabolized 95% of the AAF. Within 6 hr lung cells had metabolized 50%, and kidney cells 20%. By contrast, fibroblasts and bladder cells had metabolized only 20-25% in 24 hr. The amount of material bound to cellular components was proportional to the amount of AAF metabolized. A second measure of activation was the ability of intact organ cells to metabolize AAF to a form mutagenic in Salmonella TA 1538. Revertant numbers were much increased above background with hepatocytes (240-fold), lung cells (11-fold), intestinal cells (5-fold) and kidney cells (2-fold). With bladder cells and fibroblasts, revertant numbers were not significantly higher. We have demonstrated that intact cells, whether or not from the target organ, can metabolize AAF at a high rate to forms which either bind to cellular components or are excreted. These forms are also mutagenic in Salmonella. (no Refs)

48. ADENOSINE AND GUANOSINE 3',5' CYCLIC MONOPHOSPHATE PHOSPHODIESTERASE ACTIVITIES IN RAT SMALL AND LARGE BOWEL FOLLOWING SINGLE AND MULTIPLE EXPOSURES TO 1,2-DIMETHYLHYDRAZINE.

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Drug Chem Toxicol; 4(2):161-172 1981

The affect of the colon carcinogen, dimethylhydrazine (DMH: 20 mg/kg, sc) on the hydrolytic activities of cyclic AMP (cAMP) and guanosine 3',5'-cyclic monophosphate (cGMP) phosphodiesterases (PDE) in the small and large intestines of adult male outbred rats was determined. Following injection of DMH, an almost immediate increase in cAMP-PDE activities in the colon tissue was observed. These elevated activites, which had increased after 1 day to greater than three times that in untreated colon, returned to normal value after approx 5 days after exposure. In contrast, the cGMP-PDE activities seemed only slightly changed by the exposure to DMH. Chronic exposures at weekly intervals to the DMH had little effect on PDE activites during the early phases of tumor activity. However, at the end of wk 20, exposed colon tissues had elevated cAMP-PDE levels similar to those in cancer cells. Approx 10-15% of DMH-treated rats developed small bowel cancer. A single exposure to DMH produced a significant increase in both the cAMP- and cGMP-PDE activities. Chronic exposure to DMH resulted in little apparent PDE changes in the small intestine until approx wk 20 at which time cAMP-PDE levels were similar to those measured in small bowel tumor cells. Ratios of cAMP and cGMP and cAMP-PDE and cGMP-PDE measured in the colon tissue following single and double DMH exposure were plotted against time. The measurements suggested that cyclic nucleotide content may be a reflection of tissue insult by an environmental toxicant. (19 Refs)

49. 1,2-DIMETHYLHYDRAZINE-INDUCED CHANGES IN HEPATIC, SMALL INTESTINAL, AND COLONIC MUCOSAL CYTOCHROMES P-450 AND B5 OF RATS FED CITRUS PULP OR WHEAT BRAN.

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Drug Metab Dispos; 9(5):487-488 1981

A 3-mo feeding study showed that dietary fiber and the carcinogen 1,2-dimethylhydrazine interacted to alter hepatic and extrahepatic levels of cytochromes P-450 and b5 in liver, and small intestine and colon mucosa of male F344 rats. (16 Refs)

50. A NOTE ON THE ROLE OF DIETARY RETINOL AND CAROTENE IN HUMAN GASTRO-INTESTINAL CANCER.

Modan B, Cuckle H, Lubin F

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Int J Cancer; 28(4):421-424 1981

Dietary data relating to 406 patients with gastrointestinal cancers (cases) and 812 controls have been analyzed to test the hypotheses that dietary vitamin A (retinol) and its precursor, carotene, may be protective agents in human carcinogenesis. There was no deficit among cases in the intake of retinol-containing food items whereas several of the main carotene-containing fruits and vegetables were eaten less often among cases than among controls. However, when total daily intake was estimated, there was no protective effect of carotene, perhaps implying that some other constituent of the fruits and vegetables is protective. (Author abstract) (11 Refs)

51. EFFECT OF INDOMETHACIN ON INTESTINAL TUMORS INDUCED IN RATS BY THE ACETATE DERIVATIVE OF DIMETHYLNITROSAMINE.

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Science; 214(4520):558-559 1981

Over the course of 20 wk, Sprague-Dawley rats developed intestinal tumors in response to an ip injection of the acetate derivative of dimethylnitrosamine. The same agent did not induce tumors in Lobund-Wistar rats. The number of tumors was significantly smaller in rats given drinking water containing indomethacin (beginning 14 days after the injections) than in control rats given drug-free water. (Author abstract) (12 Refs)

BIOCHEMICAL, MORPHOLOGICAL AND IMMUNOLOGICAL ASPECTS OF GI CARCINOGENESIS

52. SUPPRESSOR T-LYMPHOCYTES WITHIN HUMAN COLON CANCER (MEETING ABSTRACT).

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Gastroenterology; 80(5,part2):1254 1981

Although peripheral blood studies of cell mediated immunity have been conducted in colon cancer patients, the relevance of these findings to tumor development is unclear. Since suppression of immunity to colon carcinoma represents a potentially important mechanism for tumor growth, the central quest ion is whether suppression of T-cell responses occurs within the cancer itself. Human colon cancers were therefore disaggregated by mechanical means involving mincing, sieving and passage through a glass bead column. The tumor-derived cell suspension was characterized and the constituent cell population separated by bovine serum albumin density gradients to yield fractions enriched for tumor cells, macrophages and lymphocytes. The T-lymphocyte population was purified by sedimentation after rosetting with sheep RBC. Suppressor activity was tested by mitogenic responses to phytohemagglutinin in co-cultures of tumor-derived cells and autologous peripheral blood lymphocytes. In 9 out of 10 separate experiments the tumor-derived cells suppressed the mitogenic response of blood lymphocytes by 30-90%. Fractionation of the tumor disaggregate into T- and non T-cell populations indicated that the suppressor activity was constantly present in the T-cell population. By contrast, the heterogeneous T-cell-depleted population was variable in its effect and on occasion, actually enhanced the response to mitogen. These data establish for the first time the existence of a dominantly suppressor T-cell population within human colon cancers, and encourage further study of the regulation of T-cell responses in this common disease. (no Refs)

53. NATURAL HISTORY OF GASTRIC CARCINOMA WITH SPECIAL REFERENCE TO THE 'EARLY CANCER' STAGE: A MITOTIC INDEX STUDY ON ORIGINAL AND RECURRENT CARCINOMAS.

Concetti HF, Kato Y, Sugano H, Kitagawa T

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Gan; 72(5):665-672 1981

The natural history of gastric carcinoma, especially during the 'early cancer' stage, was investigated in terms of chronological changes in the mitotic indices of the carcinoma. Nine cases of gastric carcinoma which recurred after long periods of time were analyzed. In seven cases in which a second operation was performed after 2 to approx 14 yr, the mitotic indices of the recurrent carcinomas were about the same as or slightly higher than those of the original ones. On the other hand, in three cases in which second operations were done within 2 yr, the mitotic indices were lower in the recurrent carcinomas. No general trend toward a change in mitotic indices, relative to either the surface topography or the depth of the stomach wall at the site of the carcinoma, was observed, although there was one exceptional case in which a distinctly elevated mitotic index was obtained at the site of the nodular down-growth of the carcinoma associated with apparent morphological features of progression. In five out of seven cases with lymph node metastasis, the mitotic indices in the metastatic site were slightly higher than in the original carcinoma. The overall impression gained from the present study was of the unchangeability of the cell kinetics of gastric carcinomas during the long early cancer stage, although the results also indicate the gradual or abrupt progression of carcinomas during their natural history. The mechanisms which produced reductions in the growth rates of carcinomas within 2 yr after operations are discussed. (Author abstract) (15 Refs)

54. THE HISTOCHEMICAL STUDY OF BETA-GLUCURONIDASE IN THE TISSUE OF GASTRIC CARCINOMA.

Chen Y

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Acta Anat Sin; 12(2):197-204 1981

The diagnostic value of increased beta-glucuronidase (BG) activity in gastric juice of gastric cancer patients has been reported. Results are described for the cytochemical analysis of BG in the tissues of gastric cancer and gastric mucosa of duodenal ulcer patients. There were 22 cases of gastric cancer and 20 cases of duodenal ulcer; resected stomach specimens were used. Using a modified Fischman's histochemical technic, it was found that gastric cancer tissues were rich in BG, with most of the enzyme distributed within the cancer cells, while lesser amount was located in the interstitial tissue. The activities of BG varied within the cancer cells, a difference being noted between well differentiated and poorly differentiated cancer cells. High BG activity was observed in a membrane-like layer covering the gastric mucosa of the cancer patients while low activity was found in the mucosa at the center of the cancer focus; the BG activity showed a marked increase in the mucosa bordering the cancer focus and in the mucosa far from it. In duodenal ulcer patients, relatively high BG activity was observed in the pyloric mucosa while relatively low activity was found in the mucosa of the body of the stomach. The significance of BG activity in gastric carcinoma is discussed (11 Refs) (In CHI)

55. MUCIN COMPOSITION AND CEA CONTENT IN ASSESSING MALIGNANT POTENTIAL OF COLONIC ADENOMAS (MEETING ABSTRACT).

Filipe MI, Abbas S, Greaves P

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Eighth European Congress of Pathology, August 30-September 4, 1981, Helsinki, Finland. The Congress 92 pp., 1981.

Adenomas are considered precursors of colo-rectal cancer yet no precise marker exists for assessing their malignant potential. We studied the variations in the composition of mucus secretion and the presence of carcinoembryonic antigen (CEA) in 74 colonic adenomas (from patients with and without synchronous colonic cancer), 22 carcinomas and adjacent 'Transitional' (Tr) mucosa. We found A) as in normal a high proportion of O-acylated sialomucins in 'Tr' mucosa and benign adenomas but its absence in polyps with malignancy and in carcinoma; and B) a progressive increase in CEA from low in 'Tr' mucosa, raising with dysplasia in adenomas to a max in carcinoma. These changes were similar in both incidental and synchronous adenomas and related to dysplasia. All controls, including normal mucosa, 8 inflammatory and 7 metaplastic polyps showed high levels of O-acylated sialomucins and minimal or absent CEA except in the metaplastic polyps where CEA was seen. These changes may be an expression of abnormal maturation or early malignant transformation and prove useful as complement to the histological criteria of premalignancy. Furthermore, they illustrate the progression of change from a pre-adenomatous state to adenoma and malignancy. (no Refs)

56. LOSS OF MUCOSAL SECRETORY COMPONENTS AND CHANGES IN GLYCOCONJUGATE COMPOSITION OF RAT COLONIC TUMORS (MEETING ABSTRACT).

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Gastroenterology; 80(5,part2):1183 1981

The aim of this study was to characterize the changes in carbohydrate composition of epithelial cell membranes (ECM) and goblet cell mucus (GCM) in transitional mucosa and benign and malignant colonic neoplasms. Colonic tumors were induced in 16 rats with 16 weekly injections of dimethylhydrazine. All animals developed neoplasms within 24 wk. Fluorescein isothiocyanate (FITC) conjugated lectins were then used to stain tissue sections from normal rats and those with tumors. Control sections were incubated with 0.3 M of the binding inhibitor to confirm specificity. Binding to N-acetyl glucosamine was measured using Wheat germ agglutinin (WGA), mannose and glucose with Concanavalin A (Con A), galactose with Ricinus communis (RCA1), sialic acid with Limulus polyphemus (LPA) and fucose with Ulex europeus (UEA1). No specific changes in lectin binding could be consistently demonstrated to ECM or to transitional mucosa. The data show that GCM and its secretory elements were absent in colonic adenocarcinoma. In benign adenomas lectin staining of GCM GlcNac, Man, Glc, Gal and Fuc residues was diminished while that of NeuNAc was unchanged; the decrease in GCM appeared to be greatest in the upper crypt. Thus alterations in GCM biosynthesis appear to correlate specifically with the degree of tumor malignancy, whereas in transitional mucosa goblet cell glyconconjugates appear normal. (no Refs)

57. CHROMOSOMES IN HUMAN LARGE BOWEL CANCER: EVIDENCE FOR NON-RANDOM CHANGES (MEETING ABSTRACT).

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Gastroenterology; 80(5,part2):1259 1981

We undertook a detailed analysis of karyotypes in large bowel cancer and correlated these observations with clinical and histological features. Cytogenetic banding studies were performed on 31 large bowel tumors, 28 of which were primary in the colon and 3 were metastatic. The 31 tumors were separable into four groups: 1) tumors with apparently normal karyotypes (3 cases), 2) tumors with simple gains of chromosomes (3 cases), 3) tumors in the near diploid range (46 chromosomes) with gains, losses, and structural aberrations (10 cases), and 4) tumors with hypotriploid-hypotetraploid karyotypes (15 case). A gain of chromosome number 8 or loss of number 17 was evident especially in the cancers with minimal karyotypic abnormality. Marker chromosomes which are easily identified by their peculiar morphology, were sometimes absent but when present ranged from simple translocations to the most complex rearrangements. There appears to be a progressive increase in chromosomal number and structural rearrangement as one progresses from proximal to distal large bowel. Of 12 patients with a family history of other epithelial cancers, 10 were in the diploid range as compared to 3 of 19 without a family history. Preliminary evidence suggests a better prognosis for patients with diploid cancers. Correlation exists between the site of the primary tumor and distinctive karyotypic patterns. The influences of environmental and genetic factors may be reflected in the differences between the diploid and hypotriploid-hypotetraploid groups. (no Refs)

58. INDUCTION OF CHANGES IN THE PEPSINOGEN CONTENT AND THE PEPSINOGEN ISOENZYME PATTERN OF THE PYLORIC MUCOSA OF THE RAT STOMACH BY SHORT-TERM ADMINISTRATION OF STOMACH CARCINOGENS.

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JNCI; 67(5):1101-1104 1981

Changes in pepsinogen isoenzyme patterns were examined in the pyloric mucosae of the stomachs of noninbred male Wistar rats after short-term administration of gastric carcinogens. N-Methyl-N'-nitro-N-nitrosoguanidine, N-ethyl-N'-nitro-N-nitrosoguanidine, and N-propyl-N'-nitro-N-nitrosoguanidine, which induce stomach cancer in rats, decreased the content of pepsinogen isoenzyme 1 (Pg 1), which was separated by polyacrylamide gel electrophoresis. They also decreased the pepsinogen content of the pyloric mucosa. 4-Nitroquinoline 1-oxide, which induces a low incidence of stomach cancer in rats, rarely decreased the Pg 1 content or the pepsinogen content of the pyloric mucosa, and the incidence of such decreases was not statistically significant. However, diethylnitrosamine and dimethylnitrosamine, which do not induce stomach cancer in rats, did not cause any decrease in pepsinogen content. Ethyl methanesulfonate, a direct-acting carcinogen used as a control, also did not decrease the pepsinogen content. (Author abstract) (15 Refs)

59. FREQUENCY AND EVOLUTION OF PRECANCEROUS AND DYSPLASTIC LESIONS OF THE STOMACH (MEETING ABSTRACT).

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Department of Pathology, Hopital A. Beclere, 92141 Clamart, France

Eighth European Congress of Pathology, August 30-September 4, 1981, Helsinki, Finland. 92 pp., 1981.

According to the World Health Organization's definition (1972) there are more risks of development of a gastric carcinoma (GC) for subjects who have precarcinomatous conditions associated or not to precancerous lesions. Those two groups of facts corresponds to a 'high-risks' population which may be especially watched over. Some of the recognized conditions concern people with gastric-stump, pernicious anemia, gastric ulcers .... The known lesions on which GC may appear, with a significantly higher frequency than in the general population are of two kinds that we will successively describe: a) proliferative lesions such as the rare diffuse or located hyperplasias (giant hypertrophic gastritis of Menetrier, gastritis cysticis profunda) and adenomatosis (polyps and polyposis). b) atrophic lesions, more frequent such as chronic gastritis or gastric atrophy. But, in these two groups of lesions the risks of GC seem to be correlated to the presence of intestinal or enterocolic metaplasia and above all to dysplasia states. It seems, so, that only the severe dysplasia could be considered as a true precarcinomatous state which can evolve to GC after impredictable and varied delay. We will describe what is known about the frequency of the precancerous conditions and lesions and the part of their responsibility among the totality of the GC. But there is still no certainty about the definition, limits and real frequency of chronic gastritis and dysplasias. We will compare and discuss our findings on biopsies and surgical specimens with literature data. (no Refs)

60. CONTRIBUTION OF HISTOPATHOLOGY TO THE CHARACTERIZATION OF PRECANCEROUS LESIONS OF THE OESOPHAGUS (MEETING ABSTRACT).

Munoz N, Crespi M

Division of Epidemiology and Biostatistics, International Agency for Research on Cancer, 150 Cours Albert Thomas, 69372 Lyon, Cedex 2, France

Eighth European Congress of Pathology, August 30-September 4, 1981, Helsinki, Finland. 92 pp., 1981.

Little is known about the precursor lesions of esophageal cancer in man. The limited number of studies are based on post-mortem or surgical specimens in the presence of unequivocal cancers, and the changes in the mucosa surrounding the tumor are assumed to be the only premalignant lesions. Thus, dysplasia has been proposed as a precancerous condition, but there is no information on lesions preceding this dysplasia. To obtain information on these lesions which will enable us to construct the history of this disease, endoscopic surveys have been carried out in two high-risk populations in northern Iran and northern China. The results obtained in these two surveys suggest that the chain of events leading to esophageal cancer commences with chronic esophagitis accompanied by atrophic changes in the epithelium, evolving in some cases to dysplasia and finally to cancer. (no Refs)

61. EPITHELIAL FOCUS ASSAY FOR EARLY DETECTION OF CARCINOGEN-ALTERED CELLS IN VARIOUS ORGANS OF RATS EXPOSED IN SITU TO N-NITROSOHEPTAMETHYLENEIMINE.

Terzaghi M, Nettesheim P, Yarita T, Williams ML

Biology Div., OakRidge Natl. Lab., P.O. Box Y, Oak Ridge, TN, 37830

JNCI; 67(5):1057-1062 1981

The purpose of these studies was to determine (a) whether epithelial cells with altered in vitro growth capacity occur not only after topical application of 7-12-dimethylbenz[a]anthracene but also after systemic administration of a carcinogenic nitrosamine, and (b) whether such cells can be isolated from tissues other than tracheal mucosa. At 3 and 20 wk following intragastric administration of 150, 300, or 600 mg N-nitrosoheptamethyleneimine (NHMI)/kg, cells were harvested from tracheas, esophagi, and lungs (target tissues for NHMI) of inbred F344 rats and seeded into culture dishes. Normal cells from nonexposed organs produced no proliferative epithelial foci (EF). Of those tracheas sampled 3 wk following exposure to 150 and 300 mg/kg, 10 and 20%, respectively, contained one or more EF that could be subcultured. Of those tracheas harvested 3 wk post exposure to 600 mg/kg or 20 wk post exposure to 150-600 mg/kg, 80-100% contained EF that could be subcultured. Twenty wk after 600 mg NHMI/kg, the incidence of tracheas harboring cell populations with neoplastic potential (agarose-positive EF) was 80%, whereas the tracheal tumor incidence determined at 24 mo was only 29%. Epithelial focus-forming units with various abnormal in vitro growth potentials were also detected in esophagi and lungs of NHMI-exposed rats. (Author abstract) (15 Refs)

62. MODIFIED PROTEIN KINASE ACTIVITY AND ISOZYME DISTRIBUTION IN ADENOCARCINOMA OF THE HUMAN COLON.

Raul F, Launay J-F, Galluser M, Doffoel M, Marescaux J, Grenier JF

Unite 61, INSERM, Ave. Moliere, Strasbourg Hautepierre, France

Biomedicine [Express]; 35(3):98-100 1981

Protein kinase activity and histone kinase isozyme distribution have been determined in soluble extracts of adenocarcinoma of the human colon and compared to adjacent normal mucosa. The results show an enhancement in endogenous protein kinase activity and the presence of an additional isozyme (PKI) for histone kinase activity in the tumor tissue. PKI activity exhibited a peculiar behavior in comparison to the isozyme PKII present in both carcinoma and normal mucosa after dialysis of the soluble extracts. It is suggested that alteration of intracellular regulatory processes involved in PKI activity might be related to the maintenance of the proliferate state in human colon carcinoma. (Author abstract) (16 Refs)

63. MUCIN HISTOCHEMISTRY OF THE COLUMNAR EPITHELIUM OF THE OESOPHAGUS: A RETROSPECTIVE STUDY.

Jass JR

Dept. Histopathology, Central Middlesex Hosp., Acton Lane, London NW10 7NS, England

J Clin Pathol; 34(8):866-870 1981

Reflux esophagitis may be accompanied by replacement of squamous epithelium by columnar epithelium (Barrett's esophagus). The columnar epithelium may resemble either gastric or intestinal mucosa, though ultrastructural and histochemical studies indicate that the intestinal type does not necessarily resemble normal small intestine. Twenty-two malignant and 10 benign esophageal specimens were examined histologically and by mucin histochemistry in an attempt to classify the various types of columnar epithelium. An incompletely differentiated variant of intestinal metaplasia secreting sulfomucins was associated with well but not poorly differentiated adenocarcinomas (p less than 0.02; Fisher's exact test). Similar findings have been described in the stomach and incomplete intestinal metaplasia may be related to disorders of growth and differentiation described in other sites such as the colon. These observations may help in the interpretation of esophageal biopsies, possibly permitting identification of patients at risk of developing esophageal adenocarcinoma. (Author abstract) (16 Refs)

PANCREATIC CARCINOGENESIS

64. NITROSAMINE-INDUCED TRANSPLANTABLE PANCREATIC DUCTAL ADENOCARCINOMA IN INBRED SYRIAN HAMSTERS.

Sindelar WF, Kurman CC
Surgery Branch, Div. Cancer Treatment, NCI, NIH, United States Dept. Health and Human Services, Bethesda, MD, 20205
JNCI; 67(5):1093-1100 1981

A pancreatic ductal carcinoma, designated CBP, was established as a transplantable tumor line in the CB/SsLak inbred strain of Syrian golden hamsters. The tumor, a primary one induced by chronic administration of the nitrosamine N-nitrobis(2-hydroxypropyl)amine, is a well-differentiated adenocarcinoma that can be propagated by transplantation in syngeneic hamsters. It grows poorly in other hamster strains. The CBP tumor develops in a predictable quantitative manner and metastasizes to regional lymph nodes. Excision of primary transplanted tumor nodules leads to immunity against subsequent secondary tumor challenges. The CBP tumor appears to be a suitable model for biologic and immunologic studies of pancreatic carcinoma in the Syrian hamster. (Author abstract) (21 Refs)

65. BIOCHEMICAL BASIS OF ACTION OF PHORBOL ESTERS ON PANCREATIC ACINAR CELLS: A NEW MECHANISM FOR STIMULATING SECRETION (MEETING ABSTRACT).

Jensen RT, Lemp GF, Gardner JD
National Institutes of Health, Bethesda, MD, 20205
Gastroenterology; 80(5,part2):1184 1981

TPA (12-O-tetradecanoyl-phorbol-13-acetate) is a potent tumor-promoting agent extracted from croton oil. In the present studies we examined the biochemical basis of action of TPA on dispersed acini from guinea pig pancreas. TPA caused a 20-fold increase in amylase secretion and was 70 percent more efficacious than a maximally effective concentration of cholecystokinin (CCK). Detectable stimulation of amylase secretion occurred with 3nM TPA, half-maximal stimulation with 0.1 uM and maximal with 30uM. The action of TPA on enzyme secretion was not altered by secretagogues that cause mobilization of cellular calcium (CCK, carbachol, bombesin, A23187) but was potentiated by secretagogues that increase cellular cyclic AMP (vasoactive intestinal peptide, secretin). TPA, however, did stimulate calcium uptake by pancreatic acini and the dose-response curve for stimulation of calcium uptake was the same as that for stimulation of enzyme secretion. These results indicate that the actions, of TPA on pancreatic acini are unique in two respects: 1) TPA is the most effective pancreatic secretagogue examined to date; 2) although the action of TPA is calcium-mediated, TPA acts by increasing the inward movement of calcium into acinar cells, not by causing mobilization of intracellular calcium. Furthermore, the close correlation between the relative abilities of phorbol esters to stimulate pancreatic enzyme secretion and the abilities of these agents to promote carcinogenesis suggests that these two effects may be caused by a common calcium-mediated mechanism. (no Refs)

66. CARCINOMA OF THE PANCREAS IN AZASERINE-TREATED RATS.

Longnecker DS
Dept. Pathology, Dartmouth Medical Sch., Hanover, NH, 03755
Am J Pathol; 105(1):94-96 1981

Pancreatic carcinomas were induced in Wistar and Lewis rats by azaserine. Tumors in early stages were characterized by atypical acinar cell nodules. Histologic types included acinar cell adenocarcinoma, undifferentiated carcinoma, microadenoma, and duct- and cyst-like carcinomas. Tumors have been maintained by serial transplantation. Comparison with human disease is made. (14 Refs)

67. THE EFFECT OF THE PANCREATIC CARCINOGEN N-NITROSO-2-METHOXY-2,6,-DIMETHYL-MORPHOLINE ON ENDOCRINE AND EXOCRINE PANCREAS OF SYRIAN HAMSTERS (MEETING ABSTRACT).

Pour PM
The Eppley Institute for Research in Cancer, Omaha, NE
Eighth European Congress of Pathology, August 30-September 4, 1981, Helsinki, Finland. 92 pp., 1981.

All nitrosamines with a pancreatic carcinogenic effect of Syrian hamsters have a common metabolite, N-nitroso(-2-hydroxypropyl) (2-oxopropyl)amine (HPOP). As the cyclic structure of this metabolite, resembling the pyranose form of the hexose-sugars and the sugar moeity of the Streptozocin (SZ), may be responsible for its affinity for the pancreas, we studied the effect of N-nitroso-2-methoxy-2,6-dimethyl nitrosomorpholine (MeNDNM), a fixed cyclic form of HPOP. We found that a single high dose of this compound exhibited, compared to the effect of SZ, selective necrosis of the B-cells of pancreatic islets with in 3 days. In surviving hamsters the islets showed signs of regeneration, which was completed within 60-72 hr. Some 40 wk later, however, and in contrast to the effect of SZ, almost all treated hamsters developed pancreatic ductular and mixed ductular-insular tumors. On the other hand, weekly application of MeNDNM in subdiabetogenic induced equivalent tumors, but did not appear to affect islet cells. These results point to the mutual response of the endocrine and exocrine pancreas to this compound, thus indicating the importance of the carcinogen's cyclic structure. Possible mechanisms involved in pancreatotropic effects of this class of chemical carcinogens will be discussed. (no Refs)

68. THE FORMATION OF N-NITROSOMETHYL(2-OXOPROPYL)AMINE FROM N-NITROSOBIS(2-OXOPROPYL)AMINE IN VIVO.

Lawson TA, Helgeson AS, Grandjean CJ, Wallcave L, Nagel D
Eppley Inst. Res. Cancer 0613, Univ. Nebraska Medical Center, 42nd and Dewey Ave., Omaha, NB, 68105
Carcinogenesis; 2(9):845-849 1981

Tissue concentrations of N-nitrosobis(2-oxopropyl)amine (BOP) and its metabolites in male Syrian golden hamsters given a single dose of BOP (10 mg/kg, sc) were analyzed by gas chromatography. BOP concentrations were higher in the pancreas than in the liver or salivary glands. N-nitrosomethyl(2-oxopropyl)amine (MOP) was present in higher concentrations in the pancreas than in the liver, and N-nitroso(2-hydroxypropyl)(2-oxopropyl)amine also was preferentially taken up by the pancreas. The results strongly suggested that MOP is a proximate carcinogenic metabolite of BOP. (15 Refs)

REVIEWS AND OTHER RELATED STUDIES

69. THE NATIONAL LARGE BOWEL CANCER PROJECT: OVERVIEW.

Copeland MM
M. D. Anderson Hospital and Tumor Inst., Univ. Texas, Houston, TX
Cancer Bull; 33(4):121-123 1981

Areas of research supported by the National Large Bowel Cancer Project are discussed. The incidence, diagnosis, and treatment of colon cancer are considered. Topics discussed in relation to large bowel cancer include the availability of suitable animal models, causation and biochemical control factors in cellular metabolism, relationship between diet and large bowel cancer, isolation and identification of mutagens/carcinogens resulting from cooking of meats and other products, chemotherapy and immunotherapy, colon cancer screening, and familial polyposis and Gardner's syndrome as models for colon carcinoma. (31 Refs)

70. ON THE CAUSES AND PREVENTION OF GASTROINTESTINAL CANCERS (MEETING ABSTRACT).

Weisburger JH
American Health Foundation, Valhalla, NY, 10595
Gastroenterology; 80(5,part2):1313 1981

The decreased incidence of gastric cancer in the United States can be traced to a lower level of gastric carcinogen ingestion as a result of lesser use of pickling and greater availability on a year-round basis of foods containing vitamin C. Colon cancer is the neoplastic disease with the highest incidence in men and women in the United States. The incidence has increased only slightly in the last 50 yr. Current evidence indicates that the disease has several risk factors. The genotoxic carcinogen may be in the brown part of fried food which is shown to be highly mutagenic and in turn contains several components. Addition of soy protein inhibits the information of mutagenic materials and may be one approach to prevention. The level of total dietary fat controls the amount of biosynthetic bile acids in the gut which, in turn, have promoting activity. The concentration of bile acids depends on dietary fat ingested and stool bulk, in turn a function of dietary fiber from cereal grains. Increasing fat raises the risk, whereas increasing fiber lowers the risk. Thus, parallel concordant results from studies in man and in animal models provide a suggestive data base for approaches to the prevention of colon cancer through 1) studying the inhibition of the formation of genotoxic carcinogens in the brown part of fried food, 2) lowering the total amount of dietary fat intake, and 3) increasing the amount of fiber intake. (no Refs)

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24. METAL-INDUCED INFIDELITY OF DNA SYNTHESIS
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Joseph Gottstein Memorial Cancer Res. Lab., Dept. Pathol., Univ. Washington, Seattle, WA, 98195
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26. METAL INTERACTIONS IN CARCINOGENESIS: ENHANCEMENT, INHIBITION
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29. EFFECTS OF METALS IN IN VITRO BIOASSAYS
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Dept. Pharmacology, Temple Univ. Sch. Medicine, Philadelphia, PA, 19140
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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service • National Institutes of Health • National Cancer Institute

20. 3173/2:

PREVALENCE OF GI CANCER IN HUMAN POPULATIONS

1. POLYPS AND COLORECTAL CANCER IN SOUTH AFRICAN BLACKS.

Segal I, Cooke SA, Hamilton DG, Tim LO
Gastroenterology Unit, Baragwanath Hosp., P. O. Berstham 2013, Johannesburg, South Africa
Gut; 22(8):653-657 1981

This study reflects the fact that cancer of the large bowel is uncommon in South African blacks, and that colorectal polyps do not appear to constitute a precursor to most colorectal cancers. Furthermore, it is shown that dietary factors associated with this cancer in western populations are not evident in the black population. In the South African white population, however, the disease behaves in a similar way to that observed in western countries. Other definitive differences found were the absence of multiple synchronous cancers and diverticular disease in the blacks with colorectal cancer. It is thus postulated that dietary factors are absent, or have not been present for a sufficient length of time to influence the development of polyps or polyp-cancer sequence in this population. It is also possible that the adenoma-carcinoma progression observed in Western countries may not be relevant to the development of all colorectal carcinomas in communities such as those reported here. (Author abstract) (19 Refs)

2. EARLY GASTRIC CANCER AT THE HOTEL-DIEU DE MONTREAL: A 30-YEAR REVIEW.

Rheault MJ, Leandri R, Lapointe A, Potvin C
Dept. Surgery, Hotel-Dieu de Montreal, 3840, rue St-Urbain, Montreal, PQ H2W 1T8, Canada
Can J Surg; 24(6):606-607 1981

Early gastric cancer is usually defined as a lesion involving the mucosa alone or the mucosa and submucosa, regardless of whether lymph-node metastases are present. Between 1948 and 1978, 1,295 gastric cancers were diagnosed at the Hotel-Dieu de Montreal. Of these, 64 (5%) were early gastric cancers. Sixty of the 64 patients underwent gastric resection for cure. The other four cancers were found incidentally at autopsy. One patient (1.7%) died following operation. Ten patients were followed up for less than 5 yr and therefore were excluded from survival analysis, as were 6 patients who died of unrelated causes. Forty-one of 43 patients survived, free of disease, for more than 5 yr following operation, a survival rate of 95.3%. The annual yield of early gastric cancers has remained relatively constant since 1948, even with a decreasing number of gastric cancers treated at the hospital. The advent of fiberoptic endoscopy significantly (p less than 0.005) increased the number of early gastric cancers detected. Further improvements will depend on a more vigorous approach to endoscopy, especially in high-risk patients. A refined radiologic technique, including double-contrast roentgenography after a barium meal, was diagnostic in all patients who underwent operation in this study. (Author abstract) (7 Refs)

3. CANCER AMONG THE FOREIGN-BORN IN NEW YORK STATE.

Nasca PC, Greenwald P, Burnett WS, Chorost S, Schmidt W
Bureau Cancer Control, New York State Dept. Health, Empire State Plaza, Albany, NY, 12237
Cancer; 48(10):2323-2328 1981

Cancer deaths among white, foreign-born residents of New York State (exclusive of New York City) during the yr 1969 through 1971 were analyzed according to country of birth. The largest numbers of immigrants came from Great Britain, Ireland, Germany, Austria, Poland, Italy, USSR, and Canada. Several distinctive features emerged from these data: Irish immigrants have an increased risk of dying from oropharyngeal, gastrointestinal, lung, and prostate cancers. Among all migrant groups studied, contrasting mortality patterns observed for carcinomas of the stomach, colon, and rectum provide further support for the concept that these neoplasms result from different etiologic processes. For the leukemias, lymphomas, and carcinomas of the breast and colon, each of the migrant groups acquired the higher risk common to others in the host country. This rise in risk suggests a major environmental component for cancers of these sites. (Author abstract) (15 Refs)

4. CANCER OF THE LUNG, STOMACH, AND PANCREAS IN SOUTHERN LOUISIANA (MEETING ABSTRACT).

Correa P, Johnson WD, Fontham ET

Louisiana State University Medical Center, New Orleans, LA

Second Annual NCI/EPA/NIOSH Collaborative Workshop: Progress on Joint Environmental and Occupational Cancer Studies, September 9-11, 1981, Rockville, Maryland. National Cancer Institute 33 pp., 1981.

With the publication of the Atlases of Cancer Mortality for US Counties: 1950-1969, it became apparent that cancer mortality rates in southern Louisiana are significantly higher than rates for the United States as a whole for all sites combined and for particular site/sex/race groupings. Studies to determine factors associated with excess risk for cancer of the lung in southern Louisiana utilizing death certificate analysis reported a two-fold excess lung cancer risk associated with certain industries in 19 south Louisiana parishes. In order to adequately assess the impact of potential risk factors on cancer of the lung, stomach and pancreas, a case-control study using an interview format to obtain detailed information on residence, occupation, tobacco usage, diet, and ancestry was determined to be the next investigative step. The purpose of this research project is to evaluate environmental determinants of cancer of the lung, stomach and pancreas in south Louisiana by a comparison of the characteristics and interview responses of cancer cases and their matched controls. The 26 parishes included in the study extend from Calcasieu parish on the Texas-Louisiana border to Orleans parish on the Mississippi-Louisiana line and from the Gulf of Mexico to the middle of the state in a north-south direction. Twenty-five hospitals are participating in the study. Outside the metropolitan New Orleans area, virtually total coverage exists. Within the metro area, a sample of public and private hospitals are included. Cases diagnosed and/or treated in any study hospital are identified and confirmed primarily through hospital pathology offices. Controls are selected from hospital admissions and are matched to cases by hospital, race, sex, and age +/-5 yr and must also be residents of the 26 study parishes. Interviewing of lung cases was completed June 30, 1981, with approx 1250 cases over the two yr period, 1979-1981. Two hundred ten stomach cancer cases and 160 pancreas cancer cases have been interviewed as of June, 1981, and interviewing will continue through Spring, 1982. Preliminary analysis of smoking histories and dietary information has begun and detailed analysis will follow. (no Refs)

5. NUTRIENT INTAKES IN RELATION TO CANCER INCIDENCE IN HAWAII.

Kolonel LN, Hankin JH, Lee J, Chu SY, Nomura AM, Hinds MW
Epidemiology Program, Cancer Center Hawaii, Univ. Hawaii, Honolulu, HI, 96813
Br J Cancer; 44(3):332-339 1981

A representative sample of 4,657 adults greater than or equal to 45 yr of age from the five main ethnic groups in Hawaii (Caucasians, Japanese, Chinese, Filipinos and Hawaiians) were interviewed during 1977-1979 regarding their diets. Quantitative food-consumption histories were obtained, from which av daily intakes of fat (saturated, unsaturated, cholesterol, meat, dairy, fish, animal, vegetable and total), protein (animal, meat, fish, dairy and total), carbohydrate, and vitamins A and C (including supplements) were calculated using food-consumption data from standard sources. Multiple regression analysis, with sex as a controlled variable, was used to assess the statistical relationship between these ethnic-sex-specific intakes and corresponding population-based cancer incidence rates of 15 selected sites for which nutrient components are suspected to be either causal or protective. Based on pre-set criteria for establishing important relationships, significant positive associations were found for 6 of the cancer sites: breast cancer with fat (saturated, unsaturated, animal, total) and protein (animal), corpus-uteri cancer with the same components as breast cancer, prostate cancer with fat (saturated, animal) and protein (animal, total), stomach cancer with fat (fish only) and protein (fish only), lung cancer with cholesterol, and laryngeal cancer with cholesterol. Breast and corpus-uteri cancers also showed significant negative associations with carbohydrate intake. The implications of these findings for future research are discussed. (Author abstract) (32 Refs)

6. CANCER INCIDENCE IN THE NETHERLANDS ANTILLES: A SURVEY COVERING THE PERIOD 1968-1979.

Freni SC, Freni-Titulaer LW
Dept. Pathology, Landslaboratorium, 55 Heelsumstraat, Curacao, Netherlands Antilles, West Indies
Cancer; 48(11):2535-2541 1981

In 1977 a retrospective study was started into the cancer incidence in the Netherlands Antilles, simultaneously with the onset of a cancer registry. This paper presents the results of this study and of the running registry, together covering a period of 12 yr. In total, 1,496 cancer cases were registered in males, and 1,480 in females. The resulting age-standardized cancer rate (World Standard Population) was 215 cases per 100,000 males and 164 cases per 100,000 females. The most frequently involved primary sites in males were, in order of frequency, lung, stomach, prostate, skin, and esophagus. Cancer in females was most frequently found in breast, uterine cervix, skin, stomach and esophagus. A comparison is made with countries inside and outside the Caribbean region, and a short comment is made on possible etiologic factors. (Author abstract) (17 Refs)

7. THE PREVALENCE OF PANCREATIC AND GASTRIC CANCERS IN A POPULATION OF HEAVY CIGARETTE SMOKERS (MEETING ABSTRACT).

Allan A, Imrie CW
Royal Infirmary, Glasgow, Scotland
Newsletter Natl Pancreas Cancer Project; VI(2):3 1981

The incidence of lung cancer and heart disease in the West of Scotland is among the highest in the world. This is mainly attributable to the high incidence of heavy cigarette smoking. In a 10 yr period from 1970, 899 gastric and 342 pancreatic cancers were diagnosed in Glasgow Royal Infirmary, with a ratio of 2.63:1.0. Histological evidence of the diagnosis was obtained in 83.3% of the gastric and 76.9% of pancreatic cancers. The proportion of ante-mortem biopsy diagnosis was 67.6% and 23.7% respectively. The male to female ratio for gastric cancer was 1.37:1.00 and 1.06:1.00 for pancreatic cancer, a lower figure than in the USA. Annual incidence of pancreatic cancer ranged from 7.1-14.7 per 100,000 with a upward trend over the decade while the more frequent gastric carcinoma ranged from 16.6-30.2/100,000, dipping in the mid-seventies to rise again at the end of the decade. Mean age for the pancreatic lesion was 63.1 and for the gastric 65.0. If pancreatic cancer is truly smoking related then the incidence of this tumor in this part of the world is surprisingly low and, while rising, is still much less common than gastric cancer. (no Refs)

8. CANCER OF THE COLON.

Audigier JC, Lambert R
Faculte de medecine, Centre d'Epidemiologie du CNRS LP005440, avenue Rockefeller, 69373 Lyon Cedex 2, France
Gaz Med Fr; 88(28):3903-3909 1981

Epidemiological factors related to colon cancer (CC) are considered. The number of CC cases increases linearly with age for both sexes. The male:female CC ratio is usually greater than 1. The genetic factor is most evident in CC developing in patients with multiple polyposis or extracolonic tumors (Gardner's syndrome). Geographic variations in the incidence of CC are described. Through the study of persons migrating from Japan or Poland to the United States, a country at high risk for CC, the importance of environment and diet in the development of CC is evident. Variations in CC incidence over time a re discussed. The risk of CC is greater in persons with polyps. The malignant potential of these adenomas varies according to the size, histological type, and degree of epithelial abnormality of the lesions. Adenomatous polyps are usually small and less likely to become malignant than are villous polyps. Patients with inflammatory intestinal disease, such as ulcerative colitis and Crohn's disease are more likely to develope CC. An excess of animal fats and cholesterol and a lack of fiber are the dietary factors most often related to the development of CC. The early detection and prevention of CC are discussed. (10 Refs) (In FRE)

9. HOW HIGH A PERCENTAGE OF ENVIRONMENTALLY RELATED CANCER CASES CAN BE PREVENTED IN NORWAY?.

Langard S
Yrkesmedisinsk avdeling, Telemark sentralsjukehus, 3900 Porsgrunn, Norway
Tidsskr Nor Laegeforen; 101(28):1602-1606 1981

Approx 110,000 cases of cancer were recorded in Norway during the period 1966-1975. Esophageal cancer was diagnosed in 1.099 cases, gastric cancer in 11,702, cancer of the gastrointestinal tract in 9,270, rectal cancer in 4,670, cancer of the liver and bile ducts in 253, pancreatic cancer in 3,992, larynx cancer in 745, lung cancer in 7,608, prostate cancer in 10,835, renal cancer in 3,191, cancer of the bladder and urinary tract in 4,047, and malignant lymphoma in 3,336. The percentage of environmentally related, ie, preventable cancer was estimated after extrapolation to the 1979 incidence. According to the low estimate, 2,250 cases of cancer were attributable to smoking, 300 to alcohol consumption, and 150 to occupational exposure. (15 Refs) (In NOR)

10. CHARACTERISTIC FEATURES OF CANCER IN TURKEY (MEETING ABSTRACT).

Firat D

No affiliation given

First UICC Conference on Cancer Prevention in Developing Countries, August 25-29, 1981, Nagoya, Japan. International Union Against Cancer 368 pp., 1981.

Although the entire characteristic features of cancer in Turkey is not fully known due to the fact that the cancer registries are not widely used, one can easily conclude from available data that the cancer is becoming one of the most important medico-social problem in this country. The statistical data of the State Institute of Statistics indicate that about 6.5% of all deaths in province and district centers of Turkey is due to the cancer. Even though this figure may well be a gross under estimate because of the fact that cancer is not a reportable disease and often the terminal event of deaths (such as heart failure, pneumonia, etc) are entered in death certificates rather than the underlying disease, the cancer is the third leading cause of death. If the 0-1 age group, where infant mortality due to infections and pneumonia is prevalant, is excluded, the cancer deaths constitute about 9.5% of all deaths as a second lead ing cause of death in Turkey. The most frequent cancer mortality in men are due to the carcinoma of the lungs and stomach (32% and 15% of all cancer deaths), while in women carcinoma of the stomach and breasts are the two leading types of cancer (16% and 6.6% of all cancer deaths). On the other hand, two separate morbidity statistics indicate that the cancer of the skin, followed by carcinoma of the breast, larynx, lungs and stomach are the most frequent types of cancers in Turkey. In pediatric age groups (0-14), acute leukemias, malignant lymphomas, bone and soft tissue tumors are the most frequent types of malignancies. There are no dependable large statistical data demonstrating geographical distribution of the cancers in Turkey at the present. (no Refs)

11. CANCER MORBIDITY IN THE USSR IN 1978.

Napalkov NP, Merabishvili VM, Tserkovnyi GF, Preobrazhenskaia MN

No affiliation given

Vopr Onkol; 27(9):3-23 1981

The incidence of various malignant tumors in the population of the Soviet Union in 1978 is reviewed. In 1978 there was a 1.2% increase in rate of overall cancer morbidity, compared with the rates for 1976 and 1977. Breast cancer moved from third place to second place in female cancer morbidity. Incidences of pharyngeal, mouth, rectal, skin, breast, lymphatic, and hematopoietic neoplasms increased in the urban population, while incidences of these cancers in the rural population decreased or remained stable. Stomach, lung, and skin neoplasms had the highest incidences; this was true in both the urban and the rural populations. The next most frequent neoplasms in the urban population were breast, lymphatic, and hematopoietic, whereas the next most frequent in the rural population were cervix, esophageal, and lip. (9 Refs) (In RUS)

12. CHARACTERISTIC FEATURES OF CANCER IN SAUDI ARABIA (MEETING ABSTRACT).

Shobokshi O

No affiliation given

First UICC Conference on Cancer Prevention in Developing Countries, August 25-29, 1981, Nagoya, Japan. International Union Against Cancer 368 pp., 1981.

Few countries are of more epidemiological interest than Saudi Arabia which is undergoing the most rapid development of any society. Malignant lymphoma appears to be the commonest of the life-threatening malignancies. There are several differences between malignant lymphoma in Saudi Arabia and the Western world, including an earlier peak of prevalence, different proportions of sub-types and the remarkable ethnic prevalence of intra-abdominal non-Hodgkin's lymphoma. More than half of solid childhood malignancies are lymphomas. Burkitt's lymphoma has been identified. Distribution of cancers of the gastro-intestinal tract is the reverse of that encountered in the West in that cancer of the mouth and esophagus are more common than cancer of the lower intestinal tract. Lung cancer is relatively uncommon. The in fluence of customs and traditions is seen in the late presentation of cancer of the female breast and in some features of cancer of the female genital tract. Finally, the well-known casual relationship between schistosoma haematobium and squamous cell cancer of the bladder has been described in Saudi Arabia. (no Refs)

13. ADVANCES IN CANCER EPIDEMIOLOGY IN SOUTH AFRICA.

Harington JS

Cancer Res. Dept., Natl. Cancer Assoc. South Africa, P.O. Box 2000, Johannesburg 2000, South Africa

S Afr Cancer Bull; 25(1/2):9-18 1981

The epidemiology of cancer in South Africa (SA) is discussed through the review of four papers on the cancer pattern in black gold miners in SA (1964-79), comparison of cancer mortality rates in SA with those of other countries, cancer mortality rates for blacks, whites, coloreds, and Asians in SA (1970-77), and the cancer problem among blacks in SA. Mortality rates were compared for all groups (SA and US: United States). Much less cancer was found in the SA urban black than in any of the other groups. The SA colored community had rates which were very nearly the highest for most of the common cancers for each site of almost all the cancers considered. The cancer pattern in SA whites of both sexes was similar to that of US whites. Whereas US blacks had consistently higher rates than US whites but the same pattern, SA blacks had a different cancer pattern to that of either the coloreds or whites in SA. The pattern for SA blacks comprised high rates for esophagus, liver, and lung cancer in males, and for cervix and esophagus cancer in females, while rates for colorectum, stomach, and female breast cancer were low. Colored males had the highest cancer risk in SA. The colored female is not nearly as much at risk as the male. Comparison between SA colored and US black males showed cancer rates to be higher in the coloreds. The overall mortality rate for cancer in SA urban blacks was lower than that for SA whites or coloreds, both males and females. The implications of these studies are discussed. (17 Refs)

14. RETROSPECT AND PROSPECT OF STUDIES ON DIGESTIVE SYSTEM DISEASES IN CHINA.

Zhang X
Dept. Internal Medicine, Capital Hosp., Chinese Acad. Medical Sciences, Beijing, People's Republic of China
Zhonghua Xiaohua Zazhi; 1(1):1-4 1981

Digestive system diseases are of frequent occurrence, but advances in their study generally lag behind those of other diseases, such as cardiovascular disease. Research on digestive system diseases in China during the past several decades and progress in this field are reviewed. Emphasis is placed on the etiology of cancers of the esophagus, stomach, liver, and colon, on their prevention, and on the combined application of modern Western medicine and traditional Chinese medicine; success in the latter is illustrated by the treatment of acute abdomen, making surgery unnecessary in such diseases as biliary calculi and gastroduodenal ulcer. Continued use of the combination of traditional medicine and modern medicine in the treatment and prevention of digestive system diseases is urged. (no Refs) (In CHI)

15. NATIONAL SURVEY OF CANCER MORTALITY IN CHINA (MEETING ABSTRACT).

Ha HW, Li B, Li J
No affiliation given
First UICC Conference on Cancer Prevention in Developing Countries, August 25-29, 1981, Nagoya, Japan. International Union Against Cancer 368 pp., 1981.

A nation-wide retrospective survey of cancer mortality for a 3 yr period was conducted in China. Three hundred and ninty-five cities and 2,136 counties were covered with a population of more than 850 million. Data were collected on mortality due to 56 causes, including 15 types of cancers. They were repeatedly checked and were considered reliable. Cancer was found to be the second and third leading causes of death among males and females. It was the first cause of death among 429 counties in the male, and among 161 counties in the female. Approx 700,000 people would die of cancer each yr in China with a crude mortality rate of 73.99 per 100,000. There were 13 provinces in China in which cancer motality rate (age adjusted to the world standard population) exceeded 100 per 100,000. In sequence of anatomic site, cancers of the upper alimentary tract were the most common. Stomach cancer occupied the first place while esophageal cancer ranked second and liver cancer was third in frequency. These three cancers accounted for 60% of all cancer deaths. In sequence among the national minorities, cancer rates were highest among the Kazak, the Hui and the Korean. The Miao and Yi tribes gave the lowest rates. Some cancers were common throughout China while others differed remarkably among the various geographical regions. These geographical distribution characteristics are to be reported in the Atlas of Cancer Mortality of the People's Republic of China. (no Refs)

16. CANCER MORBIDITY AND MORTALITY IN THAILAND (MEETING ABSTRACT).

Wiwatwong Isarangkul NA
No affiliation given
First UICC Conference on Cancer Prevention in Developing Countries, August 25-29, 1981, Nagoya, Japan. International Union Against Cancer 368 pp., 1981.

In 1977, 3,568 male and 4,628 female cancer cases were found at the NCI, the Cancer Institute Siriraj Hospital and the Ramathibodi Hospital, collectively. During the same period, there were 4,718 men and 3,659 women reported as dead due to cancer in Thailand at the Division of Health Statistics, Ministry of Public Health. It should be noted that cancers of the buccal cavity, penis and larynx, while being among the ten leading sites of cancer in men, were not among the ten leading sites of cancer death. Conversely, cancer of the brain, small intestine and leukemia were among the ten most common causes of cancer mortality but were not included in the ten most common cancers in men. In the same token, cancers of the buccal cavity, ovary and skin were among the ten leading sites but were not among the ten most common causes of cancer death in women. Again, leukemia and cancer of the brain, while being relatively rare, were included in the ten most common fatal cancers in Thai women. Although cancer was found to be the fifth reported cause of death among Thai people in 1977, it turned out to be the most common reported cause of death among those living in Bangkok in 1978. The necessity of having at least one population-based cancer registry in Thailand cannot be overemphasized. So far true cancer incidence of even a single population, let alone the whole country, has not been assessible. Any cancer prevention program without baseline cancer incidence data would be in a very haphazard situation. (no Refs)

17. CONTRIBUTION OF MIGRANT POPULATIONS TO STUDY OF CANCER RISKS (MEETING ABSTRACT).

Haenszel W

No affiliation given

First UICC Conference on Cancer Prevention in Developing Countries, August 25-29, 1981, Nagoya, Japan. International Union Against Cancer 368 pp., 1981.

The history of studies of cancer risks in migrant populations is briefly reviewed. The wide inter-country variations in site-specific cancer risk do not discriminate between hypotheses invoking differences in host characteristics or environmental exposures. Migrants represent a natural experiment which can provide information on this point. A key step was the systematic accumulation of data on risks in the countries of origin, which permitted positioning of the migrants' experience against that in 'home' and 'host' populations. This revealed important site differences in the timing and degree of transition of the migrant risks, the findings for stomach (where the migrant rates continued to resemble those in the place of origin) standing in sharp contrast to those for large bowel (where the migrant rates rise to approx those in the host population). Thus, an unanticipated, but major, outcome of the migrant studies has been to pinpoint ages of effective exposure and to contribute ideas on mechanisms. Since most of the information on migrants has come from the unidirectional movement of persons to developed countries in the Western world, the findings can provide useful clues on what may later happen to cancer risks in developing countries as they import some of the customs and environmental exposures characteristic of developed countries. While the migrant study findings have contributed little to cancer control in terms of immediate impact on cancer detection and screening procedures, their more indirect contributions by improved understandin g of etiological factors may lead later to more effective measure of disease prevention. (no Refs)

18. EPIDEMIOLOGY OF CANCERS OF THE UPPER RESPIRATORY AND DIGESTIVE TRACTS.

Le Fur R, Seng SH, Heintz J, Hernandez J
Centre Henri-Becquerel, rue d'Amiens, 76000 Rouen, France
Gaz Med Fr; 88(30):4161-4166 1981

The epidemiology of tumors of the upper respiratory and digestive tracts (URDT) is discussed. URDT cancer accounts for 8.2% of cancer mortality, 13% in men and 1.5% in women. On the av, URDT cancer occurs between 55 and 60 yr of age. Variations in the incidence of URDT cancer with time and geographic location are considered. URDT cancers can be divided into three main subsets according to site: mouth, oropharynx, and larynx; nasal fossa and bony massive of the facial nerve; and cavum. Tobacco and alcohol ingestion seem to be related to cancers of the first subset. The risk of tumors in these areas due to tobacco exposure is related to the quantity smoked and the age at which smoking was begun. Pipe and cigar smoking are less toxic than is cigarette smoking. A synergistic relationship between alcohol and tobacco intake is evident. Cancers of areas of subset I are also related to repeated microbiological infections, socioeconomic status, and occupational exposure. Dust exposure, especially that of non-resined woods, appears to be important in the development of cancers of regions of subset II. Signs of cancers of the cavum include the detection of SIN 2 antigen and Epstein Barr virus genome. (8 Refs) (In FRE)

19. EPIDEMIOLOGICAL VICISSITUDES OF LARGE INTESTINE CANCER AND OUTLOOK FOR THE FUTURE.

Hirayama T
Dept. Epidemiology, Natl. Cancer Res. Center, Tokyo, Japan
Nippon Rinsho; 39(5):10-20 1981

Age-adjusted death rates for transverse colon cancer and rectal cancer increased from 1950-1978 in Japan. In 1950 and 1978, respectively, death rates (per 100,000 population) for transverse colon cancer were 1.7 and 3.8 for men and were 2.2 and 4.1 for women; those for rectal cancer were 2.8 and 3.8 for men and 2.5 and 3.0 for women, respectively. Analysis of annual transitions of death rates by age groupings showed that death rates due to transverse colon cancer increased from 1950-1978 in all age groups, and the trend was slightly higher for men than women; except for women 40-44 yr old, death rates due to rectal cancer remained the same or decreased slightly for both men and women. By region, both age-adjusted death rates and rates of chronic disease due to transverse colon cancer showed marked increases for both men and women, and rates of increase of chronic disease due to transverse colon cancer are now 2x those for lung cancer in both men and women. Autopsy studies from 1968-1978 showed that the incidence of cancers in the sigmoid flexure increased 3.1x in men and 2.6x in women. Cigarette smokers had high death rates due to large intestine cancer, and meat eaters had low rates of death due to large intestine cancer. Extrapolation of current data indicates that death rates due to large intestine cancer will continue to rise in the future. Preventative effects of fibrous foods need to be investigated as one aspect of research on changing this trend. (no Refs) (In JPN)

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN GI CARCINOGENESIS

20. RETHINKING THE ENVIRONMENTAL CAUSATION OF HUMAN CANCER.

Higginson J
International Agency Res. on Cancer, 150 cours Albert Thomas, 69372 Lyon Cedex 2, France
Food Cosmet Toxicol; 19(5):539-548 1981

Epidemiologic studies concerning the etiology of environmental cancers are reviewed. The results of a number of studies strongly suggest that most human cancers are related to environmental factors and not to racial or hereditary factors. The results of the author's survey in South Africa further suggested that 'way of life' was of major significance for many cancers, especially those of the gastrointestinal tract and endocrine-dependent organs. Although there are many factors involved in its etiology, cancer may be prevented by controlling a single predominant factor. Only a small part of the total cancer burden can be directly related to ambient environmental pollution, and a number of other environmental factors, particularly diet, must be considered for the majority of environmental cancers. Although the role of dietary factors in promotion and enzyme induction of cancers is well established in laboratory animals, their role in man is much less clear. Most epidemiologists do not consider human environmental cancers in terms of single causes; human cancers for which there is evidence of multistage and multifactorial origin include lung, esophagus, liver, stomach and large intestine, breast and endometrium, Burkitt's lymphoma, and nasopharyngeal carcinoma. (106 Refs)

21. CHEMICAL AND ENVIRONMENTAL AGENTS IN GASTROINTESTINAL CARCINOGENESIS.

Deschner EE, De Cosse JJ, Sherlock P
Lab. Digestive Tract Carcinogenesis, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Clin Gastroenterol; 10(3):755-771 1981

A review is presented of incidence, risk factors, and chemical and environmental agents involved in induction or promotion of cancer of the gastrointestinal system. Presence of ingested agents in foods and experimental and clinical evidence for cancer causation are discussed. Carcinogenesis is considered with respect to the esophagus (nitrosamines, mycotoxins, promotional factors), stomach (nitrites and polycyclic hydrocarbons, mycotoxins, agricultural products, polychlorinated biphenyls, experimental carcinogens), and large bowel (nitrites, aflatoxins, diet, carrageenan, chemical carcinogens: nitroso compound s, biphenyls, symmetrical 1,2-dialkylhydrazines and azoalkanes and azoxyalkanes). Chemicals with known gastric tumor induction capability in animals are tabulated from published reports. (74 Refs)

22. THE HEALTH EFFECTS AND ECOLOGICAL SIGNIFICANCE OF CHLORINE RESIDUALS IN WATER.

Kalmaz EV, Kalmaz GD
Univ. Tennessee, Univ. Station 8163, Knoxville, TN, 37916
Chemosphere; 10(10):1163-1175 1981

Effects of chlorine residuals and organic compounds in drinking water and aquatic environments, particularly direct toxicity and/or carcinogenicity to human and aquatic life, are reviewed. Significant correlations between surface water chlorination and cancer mortality rates have been shown in humans. Elevated rates of bladder, rectal, colon, and gastrointestinal cancers in humans served by chlorinated water from the Mississippi River have been demonstrated. The use of chlorinated surface waters in Ohio was associated with stomach cancer in males and females, and with bladder cancer in males. Chloramine has been shown to be an extremely weak mutagen; involvement of DNA is suggested, since DNA-repair mutants are sensitive to the agent. In uremic patients, shortened RBC survival and hemolysis have been attributed to chlorinated tap water used in hemodialysis. Effects on aquatic life of chlorine residuals are reviewed. While more than 300 chlorinated organic compounds have been identified in chlorinated potable waters, cooling waters, and sanitary effluents, relatively little is known about their ecological effects. Laboratory research using animal models should focus on the chloramines and their effects on health. (65 Refs)

23. A COHORT STUDY ON CANCER AMONG WORKERS EXPOSED TO AN ANTIRUST OIL.

Jarvholm B, Lavenius B
Dept. Occupational Medicine, Sahlgrenska Sjukhuset, S-413 45 Goteborg, Sweden
Scand J Work Environ Health; 7(3):179-184 1981

An epidemiologic study of workers in an engineering company was conducted following the observation of three cases of cancer among women who wrapped bearing rings covered with antirust oil. Group A (98 persons) worked in the same packing department as the three affected women between 1954 and 1957 and were exposed to white spirit, mineral oil, lanolin, zinc naphthenate, and N-phenyl-1-naphthylamine + sodium nitrite. Group B (33) worked in another packing department and were exposed to mineral oil, vaseline, and stearic acid + sodium nitrite. Group C (31) had been treated for eczema from antirust oil in 1955 and had been exposed to white spirit, mineral oil, lanolin, zinc naphthenate, and N-phenyl-1-naphthylamine. Twelve cancers were found only among the women in Group A (expected value was 3.9 cancers); four cancers each were found in Group B and C (expected values were 2 and 3.8, respectively). The cancers in Group A were in the colon, breast, collum of the uterus (4), ovary (2), bladder, brain, thyroid, and reticulosarcoma. Two workers in Group C developed cancer of the bladder, one of whom was also included in Group A. The most likely etiological agent for Group A cancers is N-phenyl-1-naphthylamine, either alone or in combination with sodium nitrite. (15 Refs)

24. MORTALITY STUDY OF DRY CLEANERS EXPOSED TO PERCHLOROETHYLENE (MEETING ABSTRACT).

Brown DP, Kaplan S
No affiliation given
Second Annual NCI/EPA/NIOSH Collaborative Workshop: Progress on Joint Environmental and Occupational Cancer Studies, September 9-11, 1981, Rockville, Maryland. National Cancer Institute 33 pp., 1981.

A retrospective cohort mortality study was conducted to examine the long term effects from occupational exposure to perchloroethylene (PCE). This investigation was undertaken as a result of animal experiments that indicated that PCE was a carcinogen in mice. The study cohort consisted of 1,597 individuals who were employed for at least one yr before 1960 in dry cleaning shops where the primary solvent was PCE and who had no known previous occupational exposure to trichloroethylene or carbon tetrachloride. Eligible study cohort members were identified from four union locals. These records were supplemented by solvent history information on union local members shops. Of the 1,597 workers in the study, 1,058 (66.2%) were alive as of September 30, 1977, 285 (17.8%) were known dead and 254 (15.9%) were of unknown vital status. The study cohort was 64.5% female, and race was only known for deceased individuals. It was estimated that between 20-50% of the cohort was black. Conclusions regarding the risk of mortality for most causes of death are limited because of incomplete vital status ascertainment and lack of information on race. However, based on the results, cancer of the colon, which accounted for 11 observed deaths and approx 6.8 expected deaths, appears to be the cause of death most likely to have resulted from occupational exposure to PCE. It is recommended that the vital status follow-up of this cohort be updated. In addition, more accurate information on race should be added to the file before any further analysis is conducted. (no Refs)

25. NITRATE CONTENT OF DRINKING WATER AND MALIGNANT TUMORS OF THE DIGESTIVE ORGANS AND URINARY BLADDER.

Takacs S, Gomori A
Borsod megyei Kozegeszsegugyi-Jarvanyugyi Allmoas, Miskolc, Hungary
Egeszsegtudomany; 25(3):235-247 1981

Relationships between the av nitrate content in drinking water and the incidence of malignant tumors of the esophagus, stomach, large intestine, liver, rectum, and urinary bladder were studied on the basis of 2,755 cases reported during the period 1953-1980 from seven townships and five towns in a country in Hungary. There have been no appreciable changes in the nitrate levels in drinking water during the investigation period. The incidences (per 100,000 population) were 24.4 in men and 5.67 in women for esophageal tumors, 421.9 in men and 202.9 in women for gastric tumors, 84.6 in men and 78.7 in women for tumors of the large intestine, and 102.8 in men and 77.1 in women for rectal tumors. Patients in the age bracket under 40 yr accounted for 4.1% of all cases, patients in the age bracket 40-59 yr for 27.5%, and patients older than 60 yr for 68.4%. The nitrate level in the drinking water exceeded 100 mg/liter for 68.6-72.1% of the patients with digestive tract tumors, and for 54.7% of the patients with bladder tumors. The incidence of digestive tract tumors was highest at nitrate levels in the range of 100-200 mg/liter (-3.4-43%). The findings call for further epidemiological and physiological investigations. (15 Refs) (In HUN)

DIETARY AND DIGESTIVE FACTORS IN GI CARCINOGENESIS

26. NUTRITION AND CANCER: A REVIEW.

Muller E, Rickenbach M
Institut fur Sozial- und Praventivmedizin, Universitat Zurich, Gloriastrasse 32 B, 8006 Zurich, Switzerland
Praxis; 70(43):1903-1912 1981

The possible roles of various nutrients in carcinogenesis are reviewed. Epidemiological studies indicate a high rate of carcinomas of the breast (BC) and colon (CC) in industrialized countries. Dietary factors are suggested by changes in cancer frequencies among immigrant populations and their descendants. Dietary studies indicate a positive correlation between dietary fat and CC and BC, as well as a negative correlation between these cancers and dietary fiber content. Animal studies have shown a cancer-promoting effect for fats, particularly unsaturated fats. Fats may promote cancer by affecting specific intestinal bacterial populations, bile secretion, hormonal balance, and immune response. Fiber may reduce cancer risk by speeding the movement of carcinogens through the digestive tract. Cancer risk has not been confirmed for proteins or their pyrolysis products. Some studies have indicated risk associated with pickled, smoked, or fried foods related to production of nitrosamines and nitrosamides. These compounds, which have been shown to be carcinogenic, are formed in vitro from nitrites and secondary amines. Their formation appears to be limited by the presence of ascorbic acid or vitamin E. Further studies of dietary factors are indicated. (130 Refs) (In GER)

27. CHANGES IN JAPANESE EATING HABITS AND CANCER OF THE LARGE INTESTINE.

Narisawa T
First Dept. Surgery, Akita Univ. Sch. Medicine, Akita, Japan
Nippon Rinsho; 39(5):26-31 1981

Relationship between increasing rates of cancer of the large intestine and changes in eating habits by Japanese was studied with the aid of experimental animal models and review of literature. Epidemiological studies indicate that environmental and lifestyle differences account for increasing incidence of large intestine cancer more than genetic or anthropological factors. Data from experiments on producing cancer of the large intestine in rats fed either high protein (40%) and high fat (20%) diets or standard diets (20% protein, 5% fat) along with carcinogenic substances such as 1,2-dimethylhydrazine or azoxymethan supported epidemiological studies indicating that high fat and protein diets were related to high rates of cancer. Other studies on relationship of fiber content in the diet and cancer of the large intestine suggested that prolonged retention of fecal matter in the intestinal lumen increased the concentration and carcinogenic potential of secondary bile acids in fecal matter. Japanese dietary intake of fats has increased 2.2x in the past 20 yr, and concurrent with a rise in consumption of meat (50% of protein intake), the fats consumed are increasingly from animal sources instead of vegetable sources. With decreased consumption of grains, the fiber intake of Japanese had also diminished, reducing the amount of fecal matter and increasing the concentration of bile acids. (32 Refs) (In JPN)

28. OCCURRENCE OF LARGE INTESTINE CANCER AND THE ROLE OF INTRALUMINAL BACTERIA.

Hirono I
Cancerous Substances Res. Dept., Tokyo Univ. Sch. Medicine Res. Inst., Tokyo, Japan
Nippon Rinsho; 39(5):32-35 1981

Intestinal bacteria convert some of the free bile acid released into the small intestine eventually from chenodeoxycholic acid, deoxycholic acid, lithocholic acid, etc into secondary bile salts that have effects as promoters of large intestinal tumor growth. When large amounts of fats are consumed, more bile salts are released into the small intestine, and a greater amount of bile salts are potentially not reabsorbed for reuse in the liver; thus, the unabsorbed bile salts that travel into the large intestine are converted into potential carcinogenic promoters by the bacteria. The bacterial flora in the intestine and frequency of cancer of the large intestine varies according to geographic location, suggesting a causal link. Bacteria in the transverse colon can produce N-nitrosamine compounds from amines and nitric acid that is not excreted in the urine. However, if the fiber content of the feces is sufficient, the feces moves rapidly through the large bowel and direct contact of the carcinogens with the luminal wall is minimal. Roles of various types of bacteria in production of other large intestinal carcinogens have been shown, but explanations of the carcinogenic mechanisms are still being investigated. (14 Refs) (In JPN)

29. BILE ACIDS, BUT NOT NEUTRAL STEROLS, ARE TUMOR PROMOTERS IN THE COLON IN MAN AND IN RODENTS (MEETING ABSTRACT).

Weisburger JH, Reddy BS, Wynder EL
American Health Foundation, Valhalla, NY
International Symposium on Health Effects of Tumor Promotion, October 12-15, 198 1, Cincinnati, Ohio US Environmental Protection Agency and the American College of Toxicology; 1981

Colon cancer in man has distinct incidence patterns in various parts of the world. The key element distinguishing high and low populations is the intake of dietary fat and fiber. The mechanism whereby dietary fat operates in colon carcinogenesis is through control of endogenous cholesterol biosynthesis which, in turn, is the source of bile acid synthesis in the liver. Bile acids are secreted into the intestinal tract. Primary, and more so secondary bile acids were shown to be colon tumor promoters in several lines of experimentation. Dietary fat, thus, leads to specific total bile acid flow through the intestinal tract, accounting for a promoting effect. Fiber, especially cereal fiber, determines stool bulk which exerts a diluting effect on the total bile acid level in the tract. The concentration of bile acids at the mucosal barrier effectively relates to the extent of promoting action. Those findings have been made in man and animal models, thus strengthening the mechanistic concept underlying colon carcinogenesis. In most areas of the world levels of dietary fat and cholesterol relate to the risk for colon cancer and also for coronary heart disease, the latter through determining the amount of total serum cholesterol and of high density lipoprotein cholesterol. Recent instances of low serum cholesterol and apparent high colon cancer risk are accounted for by our findings, namely a higher conversion of cholestrol to bile acids acting as tumor promoters. Protection in such cases can be readily secured by ensuring an adequate intake of cereal fibers. (no Refs)

OTHER ETIOLOGIC FACTORS IN GI CARCINOGENESIS

30. EARLY IDENTIFICATION OF INDIVIDUALS AT INCREASED RISK FOR CANCER OF THE LARGE INTESTINE. PART II: DEVELOPMENT OF RISK FACTOR PROFILES.

Lipkin M, Winawer SJ, Sherlock P
Gastroenterology Service, Dept. Medicine, Memorial Sloan-Kettering Inst., New York, NY
Clin Bull; 11(2):66-74 1981

Studies to determine indices or markers identifying persons with inherited susceptibility to colorectal cancer are described. A discussion is presented of biological characteristics associated with genetic predisposition to large bowel cancer, not only during growth of benign and malignant neoplasms but also before the appearance of clinically detectable lesions. Modified epithelial cell proliferative activity may indicate predisposition. During progressive stages of abnormal development, epithelial cells gain increased ability to proliferate and accumulate in the mucosa. In subjects with familial polyposis, patches of flat mucosa are found which have colonic epithelial cells that fail to repress DNA synthesis during migration to the surface. The change occurs in normal-appearing colonic epithelial cells before and after the cells undergo adenomatous change and begin to accumulate as polyps. Observed in greater than 80% of random biopsy specimens, the failure to repress DNA synthesis has been shown to occur both in patients with polyposis coli and in certain cancer-prone families. Other early markers for increased risk of colorectal cancer are discussed. (44 Refs)

31. NON-POLYPOSIS CANCER OF THE LARGE INTESTINE.

Oohara T, Ihara O
Third Dept. Surgery, Tokyo Univ. Sch. Medicine, Tokyo, Japan
Nippon Rinsho; 39(5):60-65 1981

Risk factors for large intestine cancer were investigated by examining the intestinal mucosa of 495 patients (278 men, 217 women; 19-90 yr old) who had non-polyposis intestinal cancer. The potential for intestinal adenoma to be a site for large intestinal cancer to occur was thought to be high, but discovery was difficult owing to the small size of the lesions; 12.5% of the cases of intestinal cancer had microscopic adenomas in the mucosa surrounding the cancer which were not macroscopically observable. The cancers were thought to occur due to adenomatous changes in the basal cells of the microscopic adenomas, and 38.4-62.6% of the adenomas were observed to have such changes occurring. Residual adenoma tissues were observed in 6.7% of the advanced cancers of the large intestine. Risk of cancerous change was thought to be high even in non-polyposis large intestines if the intestinal mucosa had microscopic adenomas and the basal cells showed adenomatous changes. (20 Refs) (In JPN)

32. INCREASED RISK OF COLORECTAL CANCER AFTER CHOLECYSTECTOMY.

Turunen MJ, Kivilaakso EO
(c/o Kivilaakso) Second Dept. Surgery, Helsinki Univ. Central Hosp., Haartmaninkatu 4, 00290 Helsinki 29, Finland
Ann Surg; 194(5):639-641 1981

The relative risk of developing colorectal cancer after cholecystectomy has been assessed in a retrospective autopsy study using controls individually matched for age and sex. Of the 304 patients dying with colorectal cancer and undergoing autopsy examination at the Helsinki University Central Hospital, 45 had undergone previous cholecystectomy. The corresponding number for the matched-pair controls without colorectal cancer was 32, indicating that the relative risk of developing colorectal cancer is slightly (1.59), but significantly (p less than 0.05), increased after cholecystectomy. The relative risk was highest for cancer of the right colon (3.00). In contrast, no difference in the autopsy incidence of unoperated gallstones was observed between the two groups, suggesting that, rather than lithogenic bile alone, the predisposing factor is related to the cholecystectomy procedure itself. (Author abstract) (17 Refs)

33. TWO FAMILIES WITH CANCER FAMILY SYNDROME.

Bulow S, Svendson LB, Shannon Danes B
Kirurgisk-gastroenterologisk afdeling, Bispebjerg hospital, Copenhagen, Denmark
Ugeskr Laeger; 143(42):2716-2718 1981

Cancer family syndrome (CFS) in two families is reported. One family had 30 members in 4 generations, and reliable information is available on 29 members. Cancer was found in 11/29 cases (4 men and 7 women, age at the manifestation of the first cancer 33-38 yr, av 56 yr). The tumors included four colorectal carcinomas, four solitary colorectal adenomas, one skin cancer, two breast cancers, one gastric cancer, and one cancer of uterine cervix. Two primary cancers were found in one patient. Increased tetraploidy of skin fibroblasts, investigated in 13/29 cases, was found in 6/13 family members, 2 of whom were affected by cancer. The other family included 25 members in 4 generations; reliable information is available for 23 family members. Six members of this family, including three men and three women, had cancer: nine colorectal cancers and one retroperitoneal malignant tumor were diagnosed. There were 10 primary malignant tumors. The age of the patients at the time of manifestation of the first tumor was 37-51 yr (av 41 yr). Increased tetraploidy of kin fibroblasts, investigated in 10 family members, was found in 5/10 cases, including in 2 cancer patients. (8 Refs) (In DAN)

34. LARGE INTESTINE CANCER AND HEREDITY.

Utsunomiya J
Second Dept. Surgery, Tokyo Medical and Dental Coll., Tokyo, Japan
Nippon Rinsho; 39(5):56-64 1981

Names and classification of hereditary cancer of the large intestine, types of hereditary gastrointestinal polyposis, types of non-polyposis hereditary cancer of the large intestine, the proportion of cancers of the large intestine which are due to genetic factors, clinical distinctions and diagnosis of hereditary cancer of the large intestine, biological markers of hereditary cancer of the large intestine, and countermeasures for hereditary cancer of the large intestine were discussed. Cancers of the large intestine that are observed in family medical histories were divided into hereditary or non-hereditary types. Included in the hereditary types were hereditary gastrointestinal polyposis (adenomas of the large intestine, Peutz-Jeghers syndrome, juvenile polyposis) and non-polyposis hereditary cancer of the large intestine (non-polyposis familial cancer of the large intestine, Muir-Torre syndrome). Of 241 patients who had rectal or transverse colon cancer, 11 (4.6%) had at least one family member (parent, sibling) who had also had cancer of the large intestine; statistically, hereditary factors were thought to be involved in at least one-half of these cases. Patients with hereditary large intestine cancer had a slightly higher av age than those with adenoma and slightly lower age than those with non-hereditary cancer of the large intestine. Hereditary cancers occurred more often on the right side of the large bowel than did non-hereditary cancer. Bioma rkers for hereditary cancer of the large intestine were thought to be more definitively established for patients with polyposis than for those without polyposis. (43 Refs) (In JPN)

35. CANCER FAMILY SYNDROME.

Svendsen LB, Bulow S
Kirurgisk-gastroenterologisk afdeling, Bispebjerg hospital, Copenhagen, Denmark
Ugeskr Laeger; 143(42):2713-2716 1981

Studies on cancer family syndrome (CFS) are reviewed. CFS is characterized by high frequency of adenocarcinoma, particularly in the colon and endometrium, high frequency of multiple synchronous cancer, early development of cancer, and autosomal dominant heredity. The risk of metachronous cancer is estimated at 3%/yr of survival after the first cancer and at 6.9%/yr of survival after the second cancer. The prognosis of cancer in CFS is relatively good, which may be due partly to awareness and resulting early detection. The variants of CFS include hereditary proximal colonic cancer, hereditary solitary colonic polyp, and recessive polyposis. (30 Refs) (In DAN)

36. FAMILIAL POLYPOSIS SYNDROME.

Xiang K, Lu W, Zhang P, Chen X
Sixth People's Hosp., Shanghai, People's Republic of China
Zhonghua Xiaohua Zazhi; 1(1):74-75 1981

Familial polyposis syndrome, a precancerous condition that occurs in the colon and rectum, is often accompanied by cancerous lesions, especially at patient age of 50-60. The syndrome can occur in relatively young patients (av age, 39.2 yr) and is rapidly fatal. Clinical findings are described for six cases that occurred in two families. Diagnosis in two cases (the probands) was only established 7 yr and 9 yr after the appearance of blood in the feces. Of four cases with rectal or colonic cancer, three died within 2 yr after correct diagnosis was made. (10 Refs) (In CHI)

37. RECTOCOLIC FAMILIAL POLYPOSIS; A STUDY OF 32 CASES.

Bigay D, Plauchu H, Berard P, Robert JM, Guillemin G
(c/o Guillemin) Clinique chirurgicale C, Hotal Dieu, Place de l'Hopital, 69288 Lyon Cedex 1, France
World J Surg; 5(4):617-625 1981

Thirty-two cases of diffuse rectocolic polyposis are analyzed with respect to diagnosis, pathologic features, familial and genetic factors, surgical treatment, and relationship to development of colorectal cancer. Homogeneity of the series allows precise observations to be made on evolution and treatment of the disease. Fourteen of the 32 patients developed malignancies, most occurring in the rectum and sigmoid. Rectal resection is recommended in cases of endoscopically demonstrated local degeneration or advanced disease. (24 Refs)

38. GASTRIC STUMP CANCER AFTER PREVIOUS RESECTION FOR BENIGN ULCER.

Hellers G, Ewerth S, Ost A
Kirurgiska kliniken, Huddinge sjukhus, S-141 86 Huddinge, Sweden
Lakartidningen; 78(39):3392-3394 1981

The incidence of gastric stump cancer after gastric resection for ulcer was studied in the Stockholm area. Questionnaire data were obtained for 3,623 subjects in the age bracket 40-89 yr, who were selected at random from the population. Fifty-nine of these patients had been operated on for gastric ulcer more than 15 yr ago. They included 44 men and 15 women. A total of 709 cases of gastric cancer were diagnosed in the same area during the period 1975-1977. Eighty-seven of these patients had been submitted to gastric resection for gastric ulcer more than 15 yr ago. They included 65 men and 22 women. Their gastric cancer incidence (per 100,000 population) was 5-6 times higher than in the general population, increasing with increasing interval after resection, but not with age: the incidence was 4.5 times higher for intervals of 15-19 yr and approx 25 times higher for intervals of 40-44 yr. (7 Refs) (In SWE)

39. CANCER AFTER GASTRIC RESECTION: THE RESPONSIBILITY OF PHYSICIANS AND POLITICIANS?.

Reichard H, Ost A
Medicinklinik IV, Sodersjukhuset, Stockholm, Sweden
Lakartidningen; 78(39):3369-3370 1981

There are approx 10,000 patients in Stockholm who had been subjected to gastric resection for gastric ulcer at least 15 yr ago, including approx 3,000 under the age of 60 yr. The risk of gastric cancer in such patients is 20x higher than in the normal population of the same age, reaching about 0.5%/yr at the age of 70 yr and 1%/yr at the age of 80 yr for a patient operated on at the age of 35 yr. Radiology is of little value in the diagnosis of changes in the operated stomach, but endoscopy, preferably combined with biopsy, is efficient. Early gastric cancer can thus be detected in up to 40% of the patient, and such patients have a 5-yr survival rate of 90% after radical surgery. Yet, the incidence of early gastric cancer has been only 7% at the Stockholm hospital during the 1970s. It is recommended that all patients who had been subjected to gastric resection for gastric ulcer at least 15 yr ago, and who would qualify for gastrectomy, should be submitted to gastroscopy and gastric biopsy at 1-3 yr interval until the age of 70 yr. (5 Refs) (In SWE)

40. CARCINOGENIC TRANSFORMATION RATE OF LARGE INTESTINAL ADENOMAS AND STANDARDS TO JUDGE DEGREES OF RISK.

Kanazawa K
Dept. Surgery, Tsukuba Univ. Sch. Clinical Medicine, Ibaraki Prefecture 305, Japan
Nippon Rinsho; 39(5):47-55 1981

Autopsy was performed on 1,831 subjects since 1972, and 2,194 adenomas of the large intestine were observed. Of these 2,194, cancer in adenoma or focal carcinoma were observed in 13 specimens. Risk factors associated with the development of cancer from intestinal adenoma were assessed on the basis of these 13 specimens. Age and sex of patients with large intestinal adenoma were not related to increased risk of cancer. The larger the adenoma, the higher the risk of cancer formation. Papillotubular adenomas had significantly higher rates of cancer transformation than did tubular adenomas; the larger the tumor, the higher the chance that it was papillotubular adenoma. The cancer transformation rate of adenomas occurring in the Sigmoid flexure was significantly higher than that for adenomas occurring at other sites. When comparing the incidence of cancer, adenoma, and metaplastic polyps that occurred in particular regions of the large intestine in three matched groups of subjects, conditions for the occurrence of metaplastic polyps and cancer were correlated while those for cancer and adenomas were not correlated. Occurrence of carcinoma was more likely in patients with multiple adenomas than in those with single adenomas. Pedunculated or semi-pedunculated adenomas were also more likely to become cancerous than those that were not pedunculated. (18 Refs) (In JPN)

41. QUESTIONS CONCERNING THE CANCEROUS TRANSFORMATION OF ULCERATIVE COLITIS AND CROHN'S DISEASE.

Muto T, Konishi F, Kamiya J
First Dept. Surgery, Tokyo Univ. Sch. Medicine, Tokyo, Japan
Nippon Rinsho; 39(5):71-76 1981

Because cases of cancer combined with ulcerative colitis or Crohn's disease are rare in the Japanese literature, relationships between cancer of the large intestine and ulcerative colitis and Crohn's disease were discussed with respect to literature from the West. Of 13,987 cases of ulcerative colitis reported from 1929-1961, 563 (3.1%) were observed to be accompanied by carcinoma; combined with histological findings, a relationship between ulcerative colitis and cancer was suspected. Distinctive features of cancer associated with ulcerative colitis included a flat tumor, irregular border between the cancer and the surrounding tissue, and a high frequency of poorly differentiated carcinoma and mucin-producing carcinoma. Patients with cancer and ulcerative colitis also tended to be younger than those with cancer of the large intestine only. Patients with Crohn's disease were also thought to have a high risk of cancer, although the number of patients with cancer of the large intestine and Crohn's disease was thought to be quite small. Diagnosis of early stage large intestine cancer and precancerous conditions was thought advisable in Japan as increasing frequency of ulcerative colitis and Crohn's disease in Western countries would probably be observed in Japan in the future as well. (44 Refs) (In JPN)

42. CANCER IN ULCERATIVE COLITIS: GOOD NEWS AND BAD NEWS.

Sachar DB, Greenstein AJ
Mount Sinai Medical Center, New York, NY
Ann Intern Med; 95(5):642-644 1981

Estimation of the true incidence of colorectal cancer in ulcerative colitis is discussed, with an emphasis on the role of ascertainment bias in substantial overestimate of risk. Long-term survival in patients with colitis-associated cancer has been shown to be no worse than that in patients wi th de-novo colorectal cancer. Patients with severe dysplasia should undergo colectomy. (21 Refs)

43. ON DIVERTICULA COLI AND CANCER OF THE SIGMOID COLON.

Leao PH
Departamento de Cirurgia, Proctologicas do Hospital Geral de Fortaleza, Fortaleza, Brazil
Ceara Med; 3(2):32-33 1981

The role of diverticulitis (DS) in the etiology of colon cancer (CC) is discussed. Because 25% of CC and 90% of DS occur in the sigmoid region, the possibility of coexisting CC in DS patients should be considered. CC and DS can be observed in patients less than 40 yr old and show similar symptomatology (change in bowel habits, rectal bleeding, and left lower quadrant discomfort). Findings upon examination, surgical treatment, and pathology of CC and DS are described. (9 Refs)

INDUCTION OF GI CARCINOGENESIS IN ANIMALS

44. THE RESPONSE OF THREE INBRED STRAINS OF RAT TO THE CARCINOGEN 1,2-DIMETHYLHYDRAZINE.

Teague CA, Gavin JB, Herdson PB
(c/o Gavin) Dept. Pathology, Univ. Auckland, Private Bag, Auckland, New Zealand
Pathology; 13(3):473-485 1981

Rats of three inbred strains (DA, HS and AS2) were dosed with 1,2-dimethylhydrazine 2HCl (DMH) or saline by gavage weekly for 10 wk. DA and HS rats showed little overt toxic reaction but all AS2 rats died following DMH doses of 30 mg/kg. However, at 10 mg/kg 60% of AS2 rats survived the 30 wk experiment. All DA rats developed a high yield of adenocarcinoma of the bowel (means: males 6.8 tumors/large bowel and 0.8/small bowel; females 2.8/large and 0.08/small bowel) and one-third of the males developed tumors of the ear canal. A smaller proportion (52%) of HS rats developed tumors, specifically bowel tumors (means: male 1.4/large and 0.2/small bowel; females 0.4/large and 0.1/small bowel). Even on the lower dose of DMH AS2 rats showed extensive liver changes including cystic cholangioma (58%), angiosarcoma (25%) and hepatocellular carcinoma (8%) and 83% developed bowel tumors (means: males 2.3/large and 1.5/small bowel; females 3.5/large and 1.0/small bowel). The rapid induction and high yield of bowel tumors, the different toxicity of DMH in AS2 rats, and the differences in relative tumor density both between sexes and in the various segments of the bowel indicate the potential of these strains for studies of carcinogenesis in the bowel. (Author abstract) (32 Refs)

45 ADVANCES IN EXPERIMENTAL CANCER OF THE OESOPHAGUS.

van Rensburg SJ
Natl. Res. Inst. for Nutritional Diseases, P.O Box 70, Tygerberg 7505, South Africa
S Afr Cancer Bull; 25(1/2):66-76 1981

A review and assessment is presented of a biological program conducted during the past 15 yr. Initially acute toxicities of nitrosamines and the pathogenesis of esophageal carcinogenesis were studied. Attempts to identify carcinogens by biological means in high risk populations were largely f utile. Acute and chronic studies of nitrosamines, especially N-nitrosomethylpentylnitrosamine, in rats and primates are reported. Short-term induction of neoplasia was studied in rats. Various studies are reported which attempted to identify carcinogenic environmental agents by biologic screening methods. Rats were maintained on food from homes of esophageal cancer sufferers in rural Transkei. Snuff, tobacco and beer from the same area were also examined. Such studies yielded no esophageal carcinoma but only possibly preneoplastic changes. Studies are underway to detect possibly promoting and inhibitory actions of many minerals, vitamins and simulated staple diets on esophageal carcinogenesis, with use of a short-term induction model. A significant promoting action of even subclincal zinc deficiency has been described. There is also evidence of promoting actions of magnesium, nicotinic acid and riboflavin deficiency, as well as by high intakes of vitamin A, when other beneficial nutrients are marginally available. (15 Refs)

46. MNNG INDUCTION OF CANCER IN RESIDUAL STOMACH TISSUE.

Nishitoi H
First Dept. Surgery, Tottori Univ., Tottori, Japan
I To Cho; 16(9):942 1981

N-methly-N'-nitro-N-nitrosoguanidine (MNNG; 120 ug/ml) and 0.4% Tween 60 were administered in drinking water to male Wistar rats during mo 1-6 following hemigastrectomy, and the rats were sacrificed at mo 8. The rats were divided into four groups, based on type of surgical procedure used: Billroth-II reconstruction, Roux-Y anastomosis, gastric section, and no surgery (controls). Adenocarcinomas (primarily differentiated type) were observed in 7/18 rats subjected to Billroth-II reconstruction, 5/20 subjected to Roux-Y anastomosis, 3/20 subjected gastric section, and 2/21 serving as controls. Cancers were observed in the anastomotic site in the Billroth-II and Rous-Y group rats, in the pyloric region towards the lesser curvature in the gastric section and control rats, and throughout the region of the gastric resection in one of the rats of the gastric section group. Gastric pH of the rats subjected to Billroth-II reconstruction was high (5.1) at the time of sacrifice, those of the Rous-Y and gastric section rats were 4.5 and 2.8

respectively. Reflux of bile from the duodenum was suspected of being implicated in postgastrectomy increases in gastric pH, ulceration of the gastric anastomosis, constricting gastritis, and occurrence of cancer of the residual stomach. (no Refs) (In JPN)

47. AROCLOR 1254-INDUCED INTESTINAL METAPLASIA AND ADENOCARCINOMA IN THE GLANDULAR STOMACH OF F344 RATS.

Morgan RW, Ward JM, Hartman PE
(c/o Hartman) Dept. Biology, Johns Hopkins Univ., Baltimore, MD, 21218
Cancer Res; 41(12):5052-5059 1981

Ingestion of diets containing Aroclor 1254, a mixture of polychlorinated biphenyls, for 2 yr led to a dose-related increase in the incidence of focal lesions in the glandular stomachs of male and female F344 rats. The incidence of stomach lesions was 6% in control specimens and in specimens from rats fed a diet containing 25, 50, or 100 ppm Aroclor 1254, the incidences of stomach lesions were 10, 17, and 35, respectively. The majority of gastric lesions in treated rats were histologically identified as intestinal metaplasia characterized by an architecture resembling that of intestinal crypts and particularly by goblet cells, which stained with Alcian blue and periodic acid-Schiff reagent. Adenocarcinomas were found in six specimens. Most (88%) of the lesions were located in the pyloric region of the glandular stomach. No multiple lesions were observed among 47 control specimens examined; however, 9 cases of multiple lesions were observed in 30 lesion-containing specimens from Aroclor 1254-treated rats. Although the exact relationship between gastric intestinal metaplasia and adenocarcinoma remains to be established, they commonly coexist and may share initiating mechanisms. (Author abstract) (46 Refs)

48. DOSE RESPONSE STUDIES OF CARCINOGENESIS IN RATS BY NITROSODIETHYLAMINE.

Lijinsky W, Reuber MD, Riggs CW
Chemical Carcinogenesis Program and Information Systems Dept., Frederic Cancer Res. Center, Frederick, MD, 21701
Cancer Res; 41(12):4997-5003 1981

A dose-response study was conducted in Fischer rats with nitrosodiethylamine, which was administered in regulated amounts as a soln in drinking water. Groups of 20 female rats each received a different treatment; one group consisted of 12 animals; one of the groups was untreated. The concentrations of the soln fed ranged from 113 to 0.45 mg/liter at six successive concentrations differing by a factor of 2.5. The treatment times were 17 wk at the highest concentration; 22 wk with 45 mg/liter; and 30 wk with 18, 7, 2.8, 1.1 and 0.45 mg/liter. The two lowest dose levels were also given for 60 wk, and the 0.45-mg/liter dose levels were also given for 104 wk. Animals were allowed to die naturally with tumors, and the time to death with tumors was an index of the potency of treatment. In the top four treatment groups, the potency measured in this way was proportional to the total dose of carcinogen administered. At all other doses, survival time was much less dependent on the dose administered, whether or not tumors were induced by the treatment. The principal tumors found were in the upper gastrointestinal tract, mainly the esophagus, at all doses. In the two highest dose groups, there was a high incidence of liver tumors also. There were few liver tumors in the lower dose groups, but there was a dose-related incidence of tumors of the upper gastrointestinal tract. It was remarkable that a nitrosodiethylamine concentration of 0.45 mg/liter (0.45 ppm) administered for 104 wk induced tumors of the upper gastrointestinal tract in 70% of the treated rats. (Author abstract) (15 Refs)

49. CARCINOGENICITIES OF QUINOLINE DERIVATIVES IN F344 RATS.

Fukushima S, Ishihara Y, Nishio O, Ogiso T, Shirai T, Ito N
First Dept. Pathology, Nagoya City Univ. Medical Sch., 1 Kawasumi, Mizuho-cho Mizuho-ku, Nagoya 467, Japan
Cancer Lett; 14(2):115-123 1981

Carcinogenicity of the quinoline derivatives 6-nitroquinoline (6NQ), 8-nitroquinoline (8NQ), 6-methylquinoline (6-MQ), 8-methylquinoline (8MQ), 8-hydroxyquinoline (8HQ), and 5,7-dibromoquinoline (5,7DQ) was assayed in F344 rats. Animals were fed diets containing 0.05% 6NQ, 0.1% 8NQ, 0.05% 6MQ, 0.05%8MQ, 0.1%8HQ, or 0.1% 5,7DQ ad libitum for 104 wk or until moribund. 8NQ induced forestomach tumors in both male and female rats, including squamous cell papillomas in 28/30 males and 36/37 females, and squamous cell carcinomas in 20/30 males and 24/37 females. The other derivatives tested were not carcinogenic in F344 rats. 6NQ induced areas of focal hyperplasia in forestomach tissue. The results indicate a discrepancy between mutagenic potential of these compounds as measured in the Ames Salmonella/microsome assay and their carcinogenicity in vivo. (13 Refs)

50. THE EFFECT OF 4-SUBSTITUTION ON THE CARCINOGENICITY OF NITROSOPIPERIDINE.

Lijinsky W, Singer GM, Reuber MD
Chemical Carcinogenesis Program, Frederick Cancer Res. Center, Frederick, MD, 21701
Carcinogenesis; 2(10):1045-1048 1981

Nitrosopiperidine (NPIP), 4-phenylnitrosopiperidine, 4-cyclohexylnitrosopiperidine, and 4-tertiary-butylnitrosopiperidine were administered at equimolar (0.88) concentrations in drinking water, 5 days/wk, to groups of 20 female Fishcher 344 rats, for 50-60 wk. Like NPIP, both 4-phenyl- and 4-tertiary-butyl-NPIP induced esophageal papillomas and carcinomas in almost all animals, although time to death with tumors was considerably longer with the phenyl compound and still longer with the tertiary-butyl compound. Forestomach carcinomas occurred in 2/20 animals treated with 4-tertiary-butyl NPIP but in none of the animals treated with the other three compounds. Only 4-phenyl-NPIP induced liver tumor, 7 angiosarcomas and 14 hepatocellular carcinomas. Tongue papillomas (5) or carcinomas (7) occurred only in rats treated with 4-tertiary-butyl-NPIP. In general, NPIP induced tumors more quickly after administration of a smaller total dose than the other three compounds. The results indicate that all three derivatives of NPIP are considerably less carcinogenic than NPIP itself and that the 4-cyclo-hexyl derivative had no carcinogenic activity at the dose studied. The fact that only the 4-phenyl derivative induced liver tumors may be related to formation of phenolic compounds. (11 Refs)

MECHANISMS AND MODIFICATIONS OF GI CARCINOGENESIS

51. QUANTITATION OF A MUTAGENIC METABOLITE PRODUCED FROM 1,2-DIMETHYLHYDRAZINE DURING LIPID INFLUENCED COLON CANCER DEVELOPMENT BY A BACILLUS SUBTILIS ASSAY.

Wargovich MJ
Texas Tech University, Lubbock, TX, 79409
Diss Abstr Int [B]; 42(4):1330-B 1981

The positive correlation between intake of dietary fat and cancer of the colon is well documented. Studies were conducted using an experimental colon carcinogenesis model to determine the role of dietary fat in the metabolism of the colon carcinogen, 1,2-Dimethylhydrazine (DMH). Bacillus subtilis TKJ6321 was used to quantify fecal mutagen and postmitochondrial enzyme in the liver and the colon mucosa of rats fed diets variable in lipid content and treated ip with DMH. Corn oil or coconut oil were used as the source of lipid for the diets. During a 32 wk schedule rats were sacrificed and autopsied for evidence of adenocarcinoma of the colon. Fecal samples were extracted and assayed for mutagenic activity by B subtilis TKJ6321 as the microbial detector of mutagenicity. Rats fed corn oil in the diet and treated with DMH produced a significantly higher number of adenocarcinomas of the colon. When the lipid content of the diet was raised to 10% (wt/wt) corn oil markedly stimulated enzyme induction in animals receiving DMH treatment. This induction was especially pronounced in the mutagen-producing enzyme activity of the colonic mucosa. Treatment of rats with DMH induces enzyme in the liver and colon relevant for the conversion of this compound to a mutagenic species. The extent of enzyme activity is influenced by the type of lipid supplementing the diet as is subsequent colon tumor development. (no Refs)

52. NITRITE STABILITY AND NITROSATION POTENTIAL IN HUMAN GASTRIC JUICE.

Tannenbaum SR, Moran D, Falchuk KR, Correa P, Cuello C
Dept. Nutrition and Food Science, Massachusetts Inst. Technology, Cambridge, MA, 02139
Cancer Lett; 14(2):131-136 1981

Human gastric juice from patients free of chronic atrophic gastritis (CAG) and intestinal metaplasia (IM) was shown to contain factors which rapidly destroy nitrite. Continued generation of nitrite as a result of hypochlorhydria was found to deplete gastric juice of its protective factors and lead to an elevated rate of nitrosation. It is suggested that ascorbic acid and alpha-tocopherol may be useful in areas where gastric cancer is prevalent since these drugs destroy nitrite. (17 Refs)

53. EFFECT OF BETA-GLUCURONIDASE INHIBITOR ON AZOXYMETHANE-INDUCED COLONIC CARCINOGENESIS IN RATS.

Takada H, Hirooka T, Hiramatsu Y, Yamamoto M
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Cancer Res; 42(1):331-334 1982

In this study of the role of microfloral beta-glucuronidase in colonic carcinogenesis, the effect of beta-glucuronidase inhibitor was evaluated. Starting at 5 wk of age, male Donryu rats were fed either a semisynthetic diet or the same diet containing 0.1% beta-glucuronidase inhibitor as N-cyclohexyl-5-O-acetyl-2,4-O-(p-methoxybenzylidene)-D glucaro-1-amide-6,3-lactone (C-GAL). All animals were given sc injections of 7.4 mg azoxymethane (AOM) per kg body wt once a wk for 11 wk and followed for an additional 20 wk. Most animals receiving the colonic carcinogen developed tumors in the colon, and a few also developed tumors in the small intestine. However, the number of tumors in the large intestine of the rats given C-GAL at the same time as AOM was significantly lower than in the control rats, especially in the proximal half of the colon, but those given C-GAL after AOM treatment had almost the same number of colon tumors as did the controls. It is concluded that, since bacterial beta-glucuronidase activity in the feces of rats given 0.1% C-GAL was significantly inhibited, intestinal microfloral beta-glucuronidase may play an important role in colonic carcinogenesis caused by AOM. (Author abstract) (48 Refs)

54. EFFECT OF INHIBITORS OF TUMORIGENESIS ON THE FORMATION OF O6-METHYLGUANINE IN THE COLON OF 1,2-DIMETHYLHYDRAZINE-TREATED RATS.

Bull AW, Burd AD, Nigro ND
Wayne State Univ. Sch. Medicine, Detroit, MI, 48201
Cancer Res; 41(12):4938-4941 1981

The level of O6-methylguanine (O6MeGua) in the colonic DNA of rats treated with 1,2-dimethylhydrazine was determined. The effect of various tumorigenesis inhibitors on the formation of this modified base was also studied. Rats were given a single sc injection of 1,2-[14C]dimethylhydrazine. Six hours later, they were killed, and colonic DNA was extracted and analyzed by high-pressure liquid chromatography. The inhibitors tested were disulfiram (DSF), pyrazole, sodium selenite, butylated hydroxyanisole, butylated hydroxytoluene, potassium ascorbate, and 13-cis-retinoic acid. The level of O6MeGua in control rats was 29.9 [(O6MeGua x 10(6)/guanine)]. When rats were fed 0.25% (w/w) DSF, this value was reduced to 10.2, and at 0.5% DSF there was no detectable O6MeGua formed. Injection of pyrazole (40 mg/kg ip) 2 hr prior to 1,2-dimethylhydrazine treatment reduced the O6MeGua level to 2.4. All the other tumorigenesis inhibitors had no effect on either O6MeGua levels or the cpm/mg DNA in treated rats. With O6MeGua as a measure of the extent of initiation, these results confirm that DSF and pyrazole inhibit the initiation phase of carcinogenesis. This is to be expected as both have been shown to block the metabolism of azoxymethane, which is a crucial metabolite in the activation of 1,2-dimethylhydrazine. The other substances, all known tumorigenesis inhibitors, may act on the promotional phase of carcinogenesis and are worthy of further study for their role in cancer prevention. (Author abstract) (22 Refs)

55. DISTRIBUTION OF RADIOACTIVITY FOLLOWING ORAL ADMINISTRATION OF CARCINOGENIC 14CH 3-LABELLED NITROSOCARBARYL IN THE RAT.

Beraud M, Gaillard D, Pipy B, Derache R
Groupe de Recherches sur la Toxicologie des Aliments et des Boissons, INSERM-U87 Universite Paul Sabatier, 2 rue Francois Magendie, 31400 Toulouse, France
Cancer Lett; 14(2):169-174 1981

After a single intragastric dose of 0.25 mg/kg of 14C-N-nitrosocarbaryl (NC) to male Sprague-Dawley rats, radioactivity remaining in various organs after washing with cold NC was determined at 0.5, 3, 7, and 24 hr time intervals. Activity of the blood was high at 0.5 hr after administration and max at 7 hr. Passage of NC across the intestinal barrier was rapid. The very high % of carbaryl extracted from the blood of animals receiving NC po suggested the occurrence of denitrosation. Highest levels of radioactivity were associated with the liver, small intestine, and stomach. Activity in the various organs increased with time up to 7 hr and persisted until 24 hr, except in the forestomach where a rapid decrease was observed between 0.5 and 3 hr. However, the highest concentration of 14C-NC equivalents/mg protein was found in the forestomach. (15 Refs)

56. COMPARATIVE METABOLISM OF 2,6-DIMETHYLNITROSOMORPHOLINE IN RATS, HAMSTERS, AND GUINEA PIGS.

Underwood B, Lijinsky W
Chemical Carcinogenesis Program, Frederick Cancer Res. Center, Frederick, MD, 21701
Cancer Res; 42(1):54-58 1982

The metabolism of N-[3,5-3H]nitroso-2,6-dimethylmorpholine (NDMM) was studied in female Sprague-Dawley rats, Syrian golden hamsters, and guinea pigs. NDMM induces tumors in the esophagus in rats, pancreatic cancer in hamsters, and hemangioendothelial tumors of the liver in guinea pigs. An intragastric dose of NDMM (2 mg, 2 uCi/animal) was rapidly distributed throughout the tissues of both the rat and hamster, with no apparent accumulation of radioactivity in any one tissue. At low dose levels, NDMM was metabolized rapidly by both species. The hamster appeared to metabolize the compound faster than did the rat or guinea pig. An appreciable amount of radioactivity was excreted in the urine in all three species after 8 hr: approx 54% in the hamster; 39% in the rat; and 30% in the guinea pig. During the first 24 hr, only a small percentage of the radioactivity excreted by the hamster, rat, and guinea pig was NDMM (0.8, 2, and 0.5% respectively). High-pressure liquid chromatography analysis of urine collected 24 hr after administration revealed 12 metabolites. Although the urinary metabolites appeared to be similar in all three species, one large difference was the presence of a major urinary metabolite in hamster urine, which was absent or present in only small quantities in the rat and guinea pig. The guinea pig urine also had relatively more radioactivity present in one major fraction than did the hamster or rat. (Author abstract) (22 Refs)

57. FORMATION OF TISSUE-BOUND N'-NITROSONORNICOTINE METABOLISM BY THE TARGET TISSUES OF SPRAGUE-DAWLEY AND FISHER RATS.

Brittebo EB, Tjalve H
Dept. Toxicology, Univ. Uppsala, Box 573, S-751 23 Uppsala, Sweden
Carcinogenesis; 2(10):959-963 1981

The way in which N'-[14C]nitrosonornicotine (NNN) selectivelv induces tumors in the nasal cavity and esophagus in Sprague-Dawley and Fisher rats was investigated. No major differences in distribution of radioactivity was seen in the two strains. In vivo and in vitro autoradiographic studies following iv injection of 14C-NNN demonstrated localization of tissue-bound metabolites in the mucosa of the nasal cavity, esophagus, tracheo-bronchial tree, and tongue. High levels of unbound radioactivity were found in Zymbal's gland and submaxillary, preputial, lacrimal, and tarsal glands. In vitro experiments in which tissue slices were incubated with 3 uM 14C-NNN, demonstrated marked formation of tissue-bound NNN metabolites by nasal mucosa, liver, and esophagus. Liver tissue also formed bound NNN metabolites, but to a lesser extent than nasal mucosa, whereas levels of bound metabolites in esophagus cultures were almost undetectable. The results suggest that in situ metabolic activation of NNN plays an important role in the pathogenesis of NNN-induced tumors. (13 Refs)

58. TUMOR PROMOTION OF THE GASTROINTESTINAL TRACT OF ANIMALS: DIETARY FACTORS (MEETING ABSTRACT).

Newberne PM, Schrager T

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International Symposium on Health Effects of Tumor Promotion, October 12-15, 1981, Cincinnati, Ohio US Environmental Protection Agency and the American College of Toxicology; 1981

The biological mode of action of tumor promoters exemplified by the phorbol esters, is a subject of intensive study in a number of laboratories. A few investigators have recently begun to examine the role of dietary nutrients in tumor promotion, but the available data are sparse and interpretation difficult. A few examples are provided to indicate that some nutrients may be important in the promotion of cancer. However, the fine dividing line between effects on initiation or on promotion, so clearly shown in the mouse two-stage skin cancer model, is not so clear as yet in models used for studies in nutritional carcinogenesis. The animal models for these studies have been primarily rats, mice and hamsters. These have shown that nutrients which appear to have promotion activity are zinc deficiency and 13-cis-retinoic acid for the esophagus; vitamin A deficiency fat and vitamin A deficiency for liver and colon, lipotrope deficiency for the liver; selenium for the liver. It is probably more correct at this early stage of investigation to consider the effects of nutrients acting either during the time of administration of the carcinogen or, after such administration and when no detectible carcinogen is found in the animals tissues, rather than as promoters in the strict sense. (no Refs)

59. THE EFFECT OF DISULFIRAM ON THE CARCINOGENICITY OF 3,2'-DIMETHYL-4-AMINOBIPHENYL IN SYRIAN GOLDEN HAMSTERS AND RATS.

Fiala ES, Weisburger JH, Katayama S, Chandrasekaran V, Williams GM

Naylor Dana Inst. for Disease Prevention, American Health Foundation, Valhalla, NY, 10595

Carcinogenesis; 2(10):965-969 1981

Species differences in 3,2'-dimethyl-4-aminobiphenyl (DMAB) carcinogenicity, which induces mostly bladder tumors in Syrian hamsters and intestinal and breast tumors in rats, were investigated. Groups of male Syrian golden hamsters received sc injections of DMAB weekly for up to 22 mo (total av cumulative dose 555 mg) either alone or simultaneously with disulfiram in the diet. At the tolerated dose of disulfiram (2.5 mg/kg), the overall tumor yield induced by DMAB alone was not affected, but the number of small intestine tumors was reduced and the appearance of bladder and colon cancers was delayed. In two groups of male Charles River rats, weekly sc injection of DMAB (20 mg/kg) for 37 wk (total av cumulative dose 289 or 241 mg) induced primarily intestinal cancers. As in hamsters, addition of disulfiram to the diet of the second group reduced the incidence of small intestine cancers but resulted in the appearance of a small number of bladder cancers. DMAB-treated rats also developed in situ prostatic carcinoma, regardless of whether they were treated with or without disulfiram. (19 Refs)

60. EFFECT OF BILE ACID GAVAGE OR VAGOTOMY AND PYLOROPLASTY ON GASTROINTESTINAL CARCINOGENESIS.

Domellof L, Eriksson S, Mori H, Weisburger JH, Williams GM
Dept. Surgery, Univ. Hosp., S-901 85, Umea, Sweden
Am J Surg; 142(5):551-554 1981

Possible promotion of MNNG-induced gastrointestinal carcinogenicity was evaluated in male Wistar rats exposed to unconjugated bile acid given as gavage or as obtained through truncal vagotomy plus pyloroplasty. No significant difference was found compared with the relevant control groups. Even though gastroduodenal erosions were found more frequently in the bile acid gavage and MNNG groups than in MNNG-treated controls, secondary deconjugated bile acids apparently did not reach optimal promoting concentrations. In contrast to partial gastrectomy, vagotomy and pyloroplasty do not increase the tumor yield in the rat. (Author abstract) (23 Refs)

61. SURFACE ACTIVE AGENTS AS TUMOR PROMOTERS (MEETING ABSTRACT).

Boyland E
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International Symposium on Health Effects of Tumor Promotion, October 12-15, 1981, Cincinnati, Ohio US Environmental Protection Agency and the American College of Toxicology; 1981

Initiation and promotion are different stages in carcinogenesis. Initiators are generally mutagenic and if a substance or procedure is carcinogenic and not mutagenic the effect is most probably tumor promotion. Many carcinogens are complete, having both initiating and promoting activity. Promoters alone induce tumors because initiators are present in the diet or the environment. Promoters can be physical as with trauma and foreign bodies such as with asbestos. Promoters are often organotropic; phenobarbitone, clofibrate and valium act on the liver of rodents. Of the 14 types of tumor promoters listed, the class of surfactants includes many different compounds. Saccharin, cyclamate and tryptophan act on the rat bladder, and lithocholic acid on the colon. The sweetening agents and bile acids reduce interfacial tension by some 20% in concentrations at which they are present in urine or feces when given in doses which promote tumors in rats. The incidence of cancer of esophagus and mouth is high in smokers who consume spirits rather than beer. The cigarette provides initiators and the alcohol acts as promoter. The alcohol present in spirits would reduce the interfacial tension appreciably in the mouth and esophagus so that the carcinogenic action of spirits is probably due to the promoting action of the alcohol because of its surface activity. With promoters of the surfactant type there are levels below which the effects are negligible and so there may be safe levels. This is clearly the concentration attained at any particular time rather than the total dose. The effect of the surface active tumor promoters is probably due to action on cell membranes. The mode of action of solvents such as chloroform and benzene is probably similar. There must be safe or threshold levels for the surface active and other promoters, but probably not for materials like asbestos which remain in the body. It is possible that there are no safe levels for initiators, but if there were they might vary with exposure to promoters. (no Refs)

BIOCHEMICAL, MORPHOLOGICAL AND IMMUNOLOGICAL ASPECTS OF GI CARCINOGENESIS

62. ALKALINE PHOSPHATASE ISOZYMES FROM RAT TRANSPLANTABLE GASTRIC CARCINOMA TISSUES INDUCED BY N-METHYL-N'-NITRO-N-NITROSOGUANIDINE (MEETING ABSTRACT).

Miki K, Kobori O, Ichinose M, Miyazaki J, Iino S, Niwa H, Suzuki H, Oka H, Oda T
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Oncodev Biol Med; AbstractsBook,1:P11 1981

Experimental gastric carcinoma was developed in inbred Wistar strain rats by oral administration of N-methyl-N'-nitro-N-nitrosoguanidine, and the resulting tumor was transplanted sc into rats of the same strain. Alkaline phosphatase (ALP) isozymes were determined in these transplantable tumor tissues, and their enzymological and immunological characterizations were analyzed. They did not differ significantly until the 19th generation, and were almost the same as those of primary tumors in out-bred rats; the carcinoma tissues of rat stomach were suspected of producing high amounts of ALP isozymes (major A-band and minor B-band), especially the intestinal-type ALP isozyme (B-band). Therefore, abnormal gene expression in ALP production, especially intestinal-type ALP, seemed to be independent of the strain of rats and inherited in transplantable tumor until the 19th generation. However, after the 20th generation, specific ALP activity gradually decreased and zymogram showed almost only A-band (non-intestinal-type ALP). We propose that experimentally induced rat gastric cancer cells, initially or precancerous condition, produce the A-type of ALP isozyme, finally, as cancer cells develop, they produce the B-type, and ultimately, A plus B-type isozymes appear in the carcinoma tissues. After the 20th generation, ALP isozymes from rat transplantable tumor tissue become similar to ALP isozymes of the precancerous condition. (2 Refs)

63. MOVEMENT OF LARGE INTESTINAL MUCOSA AND ROTATION OF LARGE INTESTINAL CANCER CELLS.

Hattcri T
Pathologisches Institut der Universitat Bonn, 5300 Bonn, W. Germany
Nippon Rinsho; 39(5):36-41 1981

Cellular movement of normal large intestinal mucosa, dynamics of growth of adenomas in the large intestine, and the dynamics of proliferation of large intestinal carcinoma were discussed. 3H-TdR autoradiography showed that carcinoma cells have a longer generation time, thus effecting mitosis, than normal proliferating cells; this generation time was thought to be about 3-7 days for cancer cells compared to 24-30 hr for normal cells. Due to prolongation of cancer cell life, there are no extreme variations in the growth fraction, and cancer cells have incidental destruction. That is to say, this type of cell death is not due to maturation but rather to sudden death of the mitotic cell due to malignant change in the surrounding stroma. The time it takes for a cancer to double its vol is about 1-3 mo for human cancers in general and about 1 yr to several yr for cancers of the large intestine. (26 Refs) (Ja JPN)

64. ELECTRON MICROSCOPY OF POLYPS OF THE COLON: II. INCLUSION BODIES OF LEUCHTENBERGER.

Balazs M
Dept. Pathology, Janos Hosp., Diosarok u. 1, H-1125 Budapest, Hungary
Exp Pathol; 19(3):164-171 1981

The electron-microscopic characteristics of the Leuchtenberger's inclusion bodies were studied in adenomatous, papillary and adeno-papillary polyps of the colon. According to them, formation of intracellular inclusions is due to focal cytoplasmic degradation, and that of intercellular inclusions to the herniation of the cytoplasmic part of epithelial cells. The formation of inclusions is believed to be connected with the low stage of development of the plasma membrane of rapidly proliferating undifferentiated colonic epithelial cells. During malignant transformation of polyps, the frequently occurring inclusions are considered an important morphological sign. (Author abstract) (9 Refs)

65. RATE AND PATTERN OF EPITHELIAL CELL PROLIFERATION IN ULCERATIVE COLITIS.

Serafini EP, Kirk AP, Chambers TJ
Dept. Experimental Pathology, St. Bartholomew's Hosp. Medical Coll., London, England
Gut; 22(8):648-652 1981

We investigated the pattern of proliferation of epithelial cells in rectal mucosa taken from normal individuals and patients with ulcerative colitis by incubating mucosa with tritiated thymidine in vitro and processing for autoradiography. We found that patients with ulcerative colitis in remission showed a proliferative pattern similar to that seen in both regenerating and 'precancerous' mucosa. Patients with a short history were as likely to show this pattern as those with a long history, and this shows that the abnormal pattern does not signify impending malignant change. We also found that mucosa from patients with ulcerative colitis in remission showed an increased proportion of cells synthesizing DNA, a proportion surprisingly close to that seen in an active phase; this suggests that the abnormal pattern seen in remission is the pattern of a regenerating mucosa. We feel that this high rate of mucosal turnover, sustained not just during clinically active disease but throughout remission, leads to the increased incidence of carcinoma and to the development of carcinoma in flat mucosa. (Author abstract) (12 Refs)

66. INTESTINAL M3 ANTIGEN, A MARKER FOR THE INTESTINAL-TYPE DIFFERENTIATION OF GASTRIC CARCINOMAS.

Bara J, Hamelin L, Martin E, Burtin P
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Int J Cancer; 28(6):711-719 1981

The mucus-associated intestinal M3 antigen, normally restricted to intestinal goblet cells, was found in 35 out of 100 gastric adenocarcinomas belonging to intestinal (19/64) as well as diffuse (16/36) types according to Lauren's classification, often accompanying the other mucus-associated gastric M1 and M2 antigens. This M3 antigen was predominant over the gastric M antigens in 25 of these 35 tumors; 18 of these belonged to the histological intestinal type. According to the WHO classification, the M3 antigen was found to predominante in all mucinous adenocarcinomas (7/7), was never present in the undifferentiated carcinomas (0/8), but was also found in some tubulo-papillar (16/57) and signet-ring cell (12/27) adenocarcinomas. This antigen could be used as a new criterion and incorporated into a point system containing morphological and tumor cell behavioral considerations; then it would appear to be a good marker for intestinal-type differentiation. Indeed, 22 of these 25 gastric adenocarcinomas which produced predominantly M3 antigen showed such an intestinal-like differentiation. The M antigenic pattern of gastric carcinoma suggested a duodenal rather than colonic-type differentiation. (Author abstract) (36 Refs)

67. IMMUNOHISTOCHEMICAL EVIDENCE OF PEPTIDE HORMONES IN ENDOCRINE TUMORS OF THE RECTUM.

Alumets J, Alm P, Falkmer S, Hakanson R, Ljungberg O, Martensson H, Sundler F, Tibblin S
Dept. Histology, Univ. Lund, Biskopsgatan 5, S-223 62 Lund, Sweden
Cancer; 48(11):2409-2415 1981

Twenty-five endocrine tumors of the rectum (rectal carcinoids) were examined immunohistochemically for various pancreatic and gut neurohormonal polypeptides. Twenty-one of the tumors were found to contain cells displaying pancreatic polypeptide (PP), glucagon, somatostatin, insulin, substance P, enkephalin or beta-endorphin immunoreactivity. At least 11 of the tumors contained more than one peptide hormone. In some of the tumors PP cells made up the major cell population, in others the glucagon cells constituted the majority. Only four of the tumors contained 5-hydroxytryptamine. Rectal endocrine tumors seem unique among gut endocrine tumors in that they may store immunoreactive enkephalin, beta-endorphin and even insulin. None of the patients displayed the carcinoid syndrome; symptoms were usually vague and uncharacteristic. In many cases the tumor was found at routine examination. (Author abstract) (37 Refs)

68. PREGNANCY-SPECIFIC BETA GLYCOPROTEIN (SP1) IN TUMOURS OF THE HUMAN GASTROINTESTINAL TRACT.

Skinner JM, Whitehead R
Pathology Dept., Flinders Univ. South Australia, Bedford Park 5042, S. A., Australia
Br J Cancer; 44(3):476-478 1981

The presence of pregnancy-specific beta-glycoprotein (SP1) was studied in specimens of stomach carcinoma, colonic carcinoma, tubulovillous adenoma, and metaplastic polyp. Immunohistochemical assay showed positive staining in 9/18 cases of stomach carcinomas and in 4/17 cases of intestinal metaplasia associated with cancer. SP1 was not present in 13 cases of intestinal metaplasia with atrophic gastritis only. SP1 was present in 12/20 cases of colonic cancer, 6/22 cases of tubulovillous adenoma and 2/6 cases of metaplastic polyps. (18 Refs)

69. DETECTION OF HYALURONECTIN OR MESENCHYM ASSOCIATED ANTIGEN IN THE EARLY STAGES OF COLONIC CARCINOGENESIS INDUCED BY 1-2 DIMETHYLHYDRAZINE (MEETING ABSTRACT).

Halkin E, Delpech B, Laumonier R, Tayot J, Delapierre F
Centre Henri Becquerel, Rue d'Amiens, 76 038 Rouen Cedex, France
Oncodev Biol Med; AbstractsBook,1:P17 1981

This study dealt with the detection of a protein 'hyaluronectin' in the colon of 1,2-Dimethylhydrazine treated rats. Hyaluronectin is a hyaluronic binding glycoprotein that is associated with fetal, reactive or cancerous mesenchyme. Immunohistochemistry study used the indirect method with a n immune-serum conjugated with peroxidase. The dose dependence, the latency period of hyaluronectin production in tumors and preneoplastic lesions have been studied. It is concluded that hyaluronectin could be considered as a marker of the changes in colon tissue from the time of initiation in carcinogenesis. (no Refs)

70. GAMMA-GLUTAMYLTRANSPEPTIDASE: A TUMOR CELL MARKER WITH A PHARMACOLOGIC FUNCTION.

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Histochem J; 13(5):865-877 1981

The histochemical distribution of gamma-glutamyltranspeptidase (GGTP) in rat and human tissues is reviewed, and the changes observed during embryogenesis and carcinogenesis are discussed. The pattern of GGTP distribution is similar in both species, with activity in adults found primarily in the proximal tubules of the kidney, the secretory follicle cells of the pancreas, and the villous cells of th jejunum. There is only minimal activity in intestinal crypt cells, but considerable in mature villus cells. Mammary gland, bile duct cells in adult liver, endothelial cells of brain capillaries, follicle sheath cells in actively growing hairs, and lymphocytes also have associated GGTP activity. Higher activity is seen in both embryonal and cancerous tissues. Soon after initial exposure to carcinogens, islands of presumably preneoplastic cells form in the liver, and are characterized by very high GGTP activity. The majority of hyperplastic nodules and carcinomas that eventually develop also have increased GGTP activity. This induction of increased activity persists long after carcinogen exposure. The possible metabolic significance of GGTP is discussed. (63 Refs)

PANCREATIC CARCINOGENESIS

71. AUGMENTATION OF CARCINOGENESIS BY N-NITROSOBIS(2-OXOPROPYL)AMINE (NBOP) ADMINISTERED DURING S PHASE IN REGENERATING HAMSTER PANCREAS (MEETING ABSTRACT).

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Newsletter Natl Pancreas Cancer Project; VI(2):51 1981

It is noteworthy that ductal adenocarcinomas develop so readily in pancreas where ductal cells constitute only 4% of its vol, as contrasted to acinar cells which represent 82% of the total vol. The exclusive development of ductal adenocarcinoma in hamster following chronic exposure to carcinogens could be due to either a greater sensitivity of ductal epithelium, or to a histogenetic pathway for tumorigenesis involving acinar cells. The present experiments were undertaken to ascertain the neoplastic potential of acinar cells in hamster pancreas. This was accomplished by administering NBOP to regenerating pancreas when the max number of acinar cells are in S phase, as compared to only rare islet and duct cells. Regeneration was induced with ethionine in 30 5-6 wk old hamsters. These were divided into 2 groups, which were treated as follows: Group I 30 mg NBOP/kg body wt given at 60 hr of regeneration followed by 10 mg/kg body wt/wk for 9 wk; Group II 5 mg NBOP/kg body wt at 60 and 66 hr followed by 10 mg/kg body wt/wk for 8 wk. Three groups of animals consisting of 10 each, with normal pancreas served as controls; Group III received NBOP at doses as scheduled for Group I; Group IV received NBOP at doses as scheduled for Group II; and Group V received 10 mg NBOP/kg body wt/wk for 10 wk. Animals were sacrificed when moribund or at 26-28 wk. Pancreatic ductal adenocarcinomas were induced in all groups. However, the yield of tumor varied as follows: Grp I, 63%; Grp II, 20%; Grp III, 20%; Grp IV, 20%; Grp V, 27%. In each instance, these were invasive lesions. In many animals neoduct formation was evident in acini. The foregoing is additional support for the notion that under appropriate stimulus, acinar cells can modulate to ductal epithelium and may be involved in the development of ductal adenocarcinoma. (no Refs)

72. CARCINOMA OF THE PANCREAS IN CHILDHOOD (MEETING ABSTRACT).

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Newsletter Natl Pancreas Cancer Project; VI(2):30 1981

Current thinking is that carcinoma of the pancreas is an environmentally-related disease, a concept supported by the rarity of carcinoma in young individuals. A distinctive carcinoma of the pancreas (pancreatoblastoma, solid and papillary type) with hepatic metastases in a six-yr-old girl proceeded to her death four and a half yr later. Carcinoma of the pancreas in children occurs in these forms: 1) Adenocarcinoma analogous to that in adults, and two histologically and epidemiologically distinctive lesions, both of torpid malignancy and both related to pancreatic organogenesis; 2) Pancreatoblastoma, pleomorphic type, with acinar differentiation with or without squamous foci; and 3) Pancreatoblastoma, solid and papillary type, occurring conspicuously in adolescent or young adult women, often black. (no Refs)

73. CARCINOMA OF THE PANCREAS DEVELOPING IN CHRONIC PANCREATITIS. GENERAL REVIEW.

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Chirurgie; 107(6):459-466 1981

A review is presented of 25 published cases and one clinical case of pancreatic carcinoma developing from chronic pancreatitis. Men are more susceptible than women and are affected at a younger age (av age, 54 compared with 62 for women). The two most obvious etiological factors are alcoholism and hepatitis. It is suggested that a relationship may be proven between the two diseases when enough published cases become available. (48 Refs) (In FRE)

74. RELATIONSHIP BETWEEN PANCREATIC CARCINOMA AND CHRONIC PANCREATITIS.

Calvo F, Giura V, Carpani G, Buzzoni A, Freddi M, Ferro M, Fiora U
Divisione di Chirurgia Generale D, Ospedale Maggiore S. Giovanni Battista, Torino, Italy
Minerva Med; 72(46):3119-3121 1981

The relationship between chronic pancreatitis (CP) and pancreatic carcinoma (PC) is reviewed. Every CP may potentially be PC; all CP patients are at high risk and should be treated as such. Special attention should be given to fibrosis of intima in medium size blood vessels, structural histology in duodenal mucosa, and Brunner gland hyperplasia. (13 Refs) (In ITA)

75. A SINGLE-DOSE PROTOCOL FOR AZASERINE INITIATION OF PANCREATIC CARCINOGENESIS IN THE RAT.

Yager JD, Roebuck BD, Zurlo J, Longnecker DS, Weselcouch EO, Wilpone SA
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Int J Cancer; 28(5):601-606 1981

Previously, the induction of pancreatic carcinogenesis in the rat using azaserine has involved a multiple-dose treatment protocol. The objective of the present study was to determine the effect of multiple azaserine treatments on pancreatic DNA synthesis and to develop a protocol for a single-dose initiation of pancreatic carcinogenesis by azaserine in the rat. Pancreatic DNA synthesis in young rats, which was determined by measuring the amount of [3H]-thymidine incorporation into DNA, was found to be elevated at 4.3 wk of age and to decrease to a baseline level by 6.3 wk. Treatment of 4-wk-old rats with azaserine resulted in a dose-dependent inhibition of [3H]-thymidine incorporation into both pancreatic and liver DNA. Max inhibition was seen at 10 mg/kg body wt. This inhibition was followed by a gradual return of incorporation to normal values over a 48 hr period. One wk following pretreatment with four weekly injections of azaserine at 30 mg/kg, [3H]-thymidine incorporation into pancreatic and liver DNA was significantly elevated, suggesting that multiple injection protocols cause enhanced DNA synthesis which could have a co-carcinogenic and/or promotional effect. Single-doses of azaserine (10, 30 and 60 mg/kg) given at 7 wk of age caused the appearance of more atypical acinar cell nodules (AACN) than when given at 5 wk of age. The most effective dose was 30 mg/kg. Using alkaline elution, we determined that this response was due to the occurrence of more DNA damage in the 7-wk-old animals. Thus, these results demonstrate a rationale for the use of single-dose initiation protocols in the pancreas. An effective single-dose protocol for induction of AACN in azaserine-treated rats fed semi-synthetic diet is presented. (Author abstract) (28 Refs)

76. INDUCTION OF PANCREATIC DNA DAMAGE AND TUMORS IN RATS TREATED WITH N-NITROSO-BIS (2-OXOPROPYL)AMINE (MEETING ABSTRACT).

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Newsletter Natl Pancreas Cancer Project; VI(2):35 1981

Differences in response of various species to carcinogens pose problems in regard to extrapolation from animal experiments to man. In experimental pancreatic carcinogenesis, several oxidized derivatives of dipropylnitrosamine have been effective pancreatic carcinogens in hamsters whereas they have failed to induce pancreatic cancers in rats. In studying this species difference we have used alkaline elution analysis to demonstrate DNA damage in pancreas of rats treated with N-nitrosobis(2-oxopropyl)amine (BOP) and N-nitroso-(2-hydroxypropyl-2-oxopropyl)amine (HPOP). Because these agents were effective in inducing DNA damage in pancreas, we treated young rats with a single dose of BOP (100 mg/kg) or HPOP (20 mg/kg) and autopsied them 4 mo later. Grossly visible nodules measuring up to 3 mm were present in pancreases of rats of both groups. Histologically the pancreases contained multiple foci and nodules of atypical acinar cells which were not seen in controls. Thus, BOP and HPOP induce both DNA damage and phenotypic changes in acinar cells in rats which are similar to those induced by the pancreatic carcinogens azaserine and Ndelta-(N-methyl-N-nitrosocarbamoyl)-L-ornithine. Although rats appear to be less sensitive than hamsters to BOP, both species respond to comparable doses of HPOP. Our findings suggest that these compounds would induce pancreatic cancers in rats in studies of 1-2 yr duration if appropriate doses are given to young rats. (no Refs)

77. A STUDY OF THE EFFECTS OF 1-METHYL-1-NITROSOUREA (MNU) ON THE PHYSICAL PROPERTIES OF CHROMATIN IN THE GUINEA PIG PANCREAS (MEETING ABSTRACT).

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Newsletter Natl Pancreas Cancer Project; VI(2):67 1981

The literature indicates that carcinogens can alter the physical state of chromatin in target tissues. As a part of the study of carcinogen effects upon the pancreas and other organs, we have examined the effect of MNU administration on the thermal melting and circular dichroism spectra of pancreas and liver chromatin. Oligomeric chromatin (av DNA size 2000 base pairs) was isolated from purified nuclei by a mild nuclease digestion, followed by a 5-20% linear sucrose gradient centrifugation, and was dialyzed into 1mM Tris, pH 8 for examination of thermal melting. The melting curves were broad and when expressed in derivative form showed several distinct melting regions, with Tm values of 56, 64 and 78 C. When animals were treated with 10 mg/kg MNU, there was no effect on either the thermal melting profile or the circular dichroism spectrum of pancreatic chromatin, but with 60 mg/kg three x in eight days, there were definite shifts of melting towards lower temperatures. The effect was more pronounced in the pancreas than in the liver. There were small concurrent changes in the circular dichroism spectra. The data indicate that MNU can produce alterations in the physical state of pancreatic chromatin and that the pancreas may be more easily damaged than the liver. (no Refs)

78. MORPHOLOGIC ANALYSIS OF ATYPICAL ACINAR CELL LESIONS (AACL) INDUCED IN RAT PANCREAS BY 4-HYDROXYAMINOQUINOLINE-1-OXIDE (4-HAQO) (MEETING ABSTRACT).

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Newsletter Natl Pancreas Cancer Project; VI(2):48 1981

A metabolite and possible proximate carcinogen of 4-nitroquinoline-1-oxide, 4-HAQO, is both toxic and carcinogenic for pancreas. A single IV injection of 4-HAQO in male Wistar rats at a dose of 6 mg/kg body wt induced AACL in 100% of the animals. AACL could be classified histologically as zymogen-poor and zymogen-rich foci, and zymogen-rich nodules (grossly visible). The zymogen-poor foci contained between 20-300 cells and rarely more than 500 cells. Cells in such foci were large, contained a large irregular nucleus with a prominent nucleolus, and a markedly basophilic cytoplasm with a few to small numbers of zymogen granules. By transmission electron microscopy (TEM) these cells showed markedly irregular lateral plasma membranes, a well developed rough endoplasmic reticulum (RER) and a few zymogen granules. Cells in zymogen-rich foci and nodules were arranged in acini which were larger than adjacent acini. The cells contained an intensely eosinophilic granular cytoplasm, and a large oval basophilic nucleus with a prominent nucleolus. By TEM, the cells showed a zymogen rich cytoplasm, RER and irregular lateral membranes. The mitotic and [3H] thymidine labeling indices respectively of both cell variants of AACL were as follows: eosinophilic cells, 2.75 and 23.2 basophilic cells 0.125 and 1.2 as compared to 0 and 1 for normal pancreatic acinar cells. These studies indicate that 4-HAQO induces at least 2 varients of AACL with different morphological features and growth potential. Their role in the pathogenesis of acinar cell adenomas and carcinomas remains to be elucidated. (no Refs)

79. TISSUE AND SPECIES DIFFERENCES IN THE ABILITY OF THE PANCREATIC CARCINOGEN N-NITROSOBIS(2-OXYPROPYL)AMINE (BOP) TO INDUCE DNA DAMAGE (MEETING ABSTRACT).

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Newsletter Natl Pancreas Cancer Project; VI(2):32 1981

The production of DNA damage is a measure of a carcinogen's ability to induce potentially mutagenic and carcinogenic lesions in DNA. The ability of the carcinogen BOP to produce such lesions has been compared in target and non-target tissues of Syrian hamsters and MRC rats. In hamsters, BOP's carcinogenicity was dose-dependent, producing only pancreatic tumors at lower doses and also liver tumors at higher doses. In rats, BOP's carcinogenicity depended on the route of administration, and resulted in liver and colo-rectal tumors when given sc and prostate tumors when given po. Extensive DNA damage was produced in hamsters by 10 mg BOP/kg in the pancreas (target tissue) and the liver and salivary gland (non-target tissues). BOP persisted longer in the pancreas. At higher doses (20 and 40 mg/kg) persistance of damage was also seen in the liver. For the DNA damage in the pancreas there was an impressive dose response and a close correlation with the carcinogenicity of BOP. In rats, no DNA damage was seen in the pancreas (non-target tissue). The tissues in which BOP is a carcinogen all exhibited extensive and persistent DNA damage (liver, colon and prostate). These studies are being complemented by examinations of the in vivo metabolism of BOP and the nature and extent of alkylation produced. These results indicate that a potent carcinogen such as BOP is capable of producing potentially carcinogenic lesions in a variety of tissues, but that the subsequent carcinogenicity depends on one or more other factors, such as the capacity to produce a mitogenic response which will stimulate the tissue to cell division to 'lock in' the carcinogenic lesion. (no Refs)

80. A STUDY OF THE ORGAN DISTRIBUTION AND BINDING OF 1-METHYL-1-NITROSOUREA (MNU) AND 1-METHYL-3-NITRO-1-NITROSOGUANIDINE (MNNG) AFTER ORAL ADMINISTRATION IN THE GUINEA PIG (MEETING ABSTRACT).

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Newsletter Natl Pancreas Cancer Project; VI(2):67 1981

The induction of pancreatic carcinoma in the guinea pig by the oral administration of MNU is an important animal model for this disease. Much of our effort is directed at an analysis of this system and at a comparison of MNU with the related compound MNNG, which is a gastric carcinogen rather than a pancreatic carcinogen after oral administration. In this study we have compared directly the distribution of these two agents in the guinea pig. Each drug synthesized with 14C in either the methyl group or the carbonyl (guanidino) carbon and these separate preparations were given as a single oral dose of 0.1 mmoles/kg body wt. Organ uptake as a function of time was expressed as total and acid-insoluble radioactivity. Alkylation was estimated as the radioactivity in DNA, RNA and protein fractions and confirmed by measuring the formation of 7-methylguanine on high pressure liquid chromatography. Widespread distribution of these drugs was measurable. Highest levels of all 4 drug labels were found in the liver. For other organs, including the pancreas, peak whole tissue levels ranged from 10-50 nmoles/g, of which 20-30% was TCA-precipitable. In the stomach, alkylation of DNA and RNA was comparable for MNU and MNNG, but in all other organs MNU binding was 2-10 fold greater than MNNG. This difference was very evident in the pancreas. Binding of MNU in the pancreas was comparable to that in other organs and persisted at least 24 hr. The data show that the pancreas and other organs are readily modified by the oral administration of MNU. They support the idea that MNU would be a more potent pancreatic carcinogen than MNNG, in agreement with earlier data in pancreatic lobules. (no Refs)

81. METABOLISM OF N-NITROSO-2,6-DIMETHYLMORPHOLINE (NNDM) BY THE VARIOUS COMPONENT CELLS OF HAMSTER PANCREAS (MEETING ABSTRACT).

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Newsletter Natl Pancreas Cancer Project; VI(2):52 1981

Hamster pancreas contains the necessary enzymes for activation of NNDM and N-nitrosobis(2-oxopropylamine) (NBOP) to forms mutagenic for Salmonella typhimurium. We report here on the metabolism of [3H]NNDM by S-9 and microsomes of whole pancreas (WP), and highly purified fractions of acinar cells (AC), and S-9 of islet cells (IC) isolated from normal and tetrachlorodibenzoparadioxin (TCDD) treated pancreas. Metabolism by duct and ductal cells was established by incubation of pancreatic slices in medium containing NNDM in the presence of [3H] thymidine with and without hydroxyurea to assess DNA repair. Analysis of metabolites by high pressure liquid chromatography showed that S-9 of WP, AC and IC metabolize NNDM to the following sequences of compounds respectively in descending order of concentration: N-nitroso(2-hydroxypropyl-2-oxopropyl)amine (HPOP) greater than NBOP greater than nitrosobis(2-hydroxypropyl)amine (BHP); NBOP greater than HPOP greater than BHP; and NBOP greater than BHP greater than HPOP. Addition of NADPH did not significantly alter metabolism of WP, but for AC led to increased formation of BHP; pretreatment with TCDD increased total metabolism in all instances. Microsomes of WP and AC produced the sequence NBOP greater than BHP greater than HPOP. TCDD increased (78%) total metabolism over that of controls. NADPH led to increased metabolism with both control microsomes (228%) and those isolated from TCDD pretreated animals (212%). Metabolism by S-9 and microsomes isolated from WP, AC and IC were about 1/20 those isolated from liver. Unscheduled DNA synthesis (repair) in nuclei of duct epithelium suggests that these cells are also capable of metabolizing NNDM. (1 Ref)

82. CHARACTERIZATION OF BENZOPYRENE HYDROXYLASE ENZYME ACTIVITY IN RAT PANCREAS (MEETING ABSTRACT).

Black O

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Newsletter Natl Pancreas Cancer Project; VI(2):11 1981

The increasing incidence of pancreatic cancer, the growing environmental pollution problems, and our increased knowledge of interactions of various exogenous factors such as diet, sex, etc, heightens the need for information on etiology of pancreatic cancer. There are presently several models of carcinogen-induced cancer. Establishment of the capability of tissue to form active intermediates is necessary to establish a relationship between exposure to carcinogens and subsequent tumorigenic response. The present studies were undertaken to characterize the pancreatic metabolic system, specifically that which metabolizes the ubiquitous carcinogen, benzopyrene (BP). We determined the Km and Vmax of the BP hydroxylase enzyme reaction in male Sprague Dawley rats pretreated with 20 mg/kg 3-methylcholanthrene (3MC), 75 mg/kg phenobarbital (PB), or solvent as control. Type of cytochrome involved was examined by measuring the reaction in the presence of 7,8-benzoflavone (BF), an inhibitor of the cytochrome P-448-related enzyme activity. The data indicated that the enzyme activity was induced by pretreatment with PB but not with 3MC. These pretreatment protocols resulted in changes both in Km and Vmax. Studies with BF suggested that pancreatic tissue contained only one hemoprotein and point out species differences between the rat and guinea pig. These studies confirm the pancreatic capability to metabolize procarcinogens and to further degrade carcinogenic metabolites, and strengthens the role of carcinogen exposure in the etiology of pancreatic cancer. (no Refs)

83. EFFECT OF CAFFEINE (CF) ON PANCREATIC CARCINOGENESIS OF 4-HYDROXYAMINO-QUINOLINE 1-OXIDE (4-HAQO) IN RATS (MEETING ABSTRACT).

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Newsletter Natl Pancreas Cancer Project; VI(2):31 1981

Sixty male Wistar rats weighing 160 g were used. 4-HAQO, at a dose of 7 mg/kg was given by iv injection and CF was given by sc injection for 12 hr intervals. Group (G) 1 received 4-HAQO at 3 days after partial pancreatectomy (PP) G 2 received 6 x injections of 120 mg/kg of CF before 4-HAQO which was given 3 days after PPGs 3, 4, and 5 received 12 x injections of 120, 60, and 30 mg/kg of CF after 4-HAQO which was given 3 days after PP, respectively. All rats were sacrificed at 52 wk, and examined macroscopically and histologically. The numbers of pancreatic tumors counted macroscopically were 14.9 +/-6.6 in G 1, 10.0 +/-5.9 in G 2, 6.0 +/- in 3.2 G 3, 22.7 +/-8.3 in G 4, and 28.1 +/-11.4 in G 5. These results suggest t hat CF showed biphasic effects, inhibitory and enhancing ones, on the pancreatic carcinogenesis of 4-HAQO in rats. (no Refs)

84. EFFECTS OF THE INTERACTION OF DIETARY FAT AND PROTEIN ON EXPERIMENTAL PANCREATIC CANCER IN SYRIAN HAMSTERS (MEETING ABSTRACT).

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Newsletter Natl Pancreas Cancer Project; VI(2):10 1981

The effects of dietary protein on pancreatic carcinogenesis by N-nitrosobis-(2-oxopropyl)amine (BOP) in the Syrian hamster were evaluated at three dietary fat levels. In previous reports we demonstrated enhanced pancreatic ductular carcinoma yield as the dietary fat level rose. Syrian hamsters were fed three levels of dietary protein (P) as casein [9 low (LP), 18 medium (MP) and 36 high (HP) g/385 Kcal] with each of three levels of fat (F) as corn oil [4.5 low (LF), 9.0 medium (MF) and 18.0 high (HF) g/385 Kcal] either before (3-7 wk of age) or after (8 wk-death) treatment with a single injection (10 mg/kg sc) of BOP. Carcinoma yields were modified by diet only in hamsters fed the various diets after BOP administration. The enhanced carcinoma yield with increasing fat intake after BOP as observed at the MP level was also seen at the HP level in both sexes [HP-LF, 7/47 (15% incidence); HP-HF, 19/55 (35% incidence)]. Effects of dietary protein on carcinoma incidence were observed at the MF level in females [LP-MF, 0/28 (0%); HP-MF, 8/27 (30%)], but not in males [LP-MF, 10/29 (34%); HP-MF, 5/24 (21%)]. In hamsters fed the HF diets the lowest protein level resulted in a decrease in carcinoma yield [LP-HF, 1.5 carcinomas/total body area (TBA); HP-HF, 3.6 carcinomas/TBA]. Pancreatic adenomas were influenced by dietary fat and protein levels before or after BOP treatment. Feeding the low protein diets dramatically reduced adenoma yield, particularly at the high fat level. For example, feeding LP-HF and HP-HF diets to male hamsters resulted in 8 and 14 adenomas/TBA respectively when fed before BOP and 15 and 31 adenomas/TBA when fed after BOP. (no Refs)

85. MODIFYING FACTORS IN PANCREATIC CARCINOGENESIS IN THE SYRIAN HAMSTER MODEL. I. THE EFFECT OF DUCT LIGATION AND PARTIAL PANCREATECTOMY (MEETING ABSTRACT).

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Newsletter Natl Pancreas Cancer Project; VI(2):47 1981

By examining the effect of pancreatic duct ligation and partial pancreatectomy on the overall pancreatic carcinogenicity of a single injection of N-nitrosobis(2-oxopropyl)amine (BOP), it was found that the incidence and the multiplicity of tumors were significantly decreased after both types of surgery when BOP was given immediately after the wound closure, but not when BOP was given later, ie after 3 days or 1 wk. For example, 62% of all hamsters treated with BOP one wk after partial pancreatectomy developed tumors, whereas only 8% of those receiving the same dose immediately after surgery showed the equivalent neoplasms. In comparison, a 60% tumor incidence occurred in hamsters not operated upon or which received the carcinogen later than 3 days after the surgery. It is interesting that a similar pattern was also observed in sham-operated BOP-treated hamsters. The pattern of benign and malignant tumors induced by each procedure will be presented, and the possible reasons for inhibition of tumor development by surgery will be discussed. (no Refs)

86. PROTECTIVE EFFECT OF ETHANOL ON THE DEVELOPMENT OF PANCREATIC CANCER (MEETING ABSTRACT).

Tweedie JH, Reber HA, Pour P
No affiliation given
Newsletter Natl Pancreas Cancer Project; VI(2):61 1981

We examined the effects of chronic ethanol ingestion on pancreatic function and the appearance of pancreatic neoplasms in hamsters. Three groups of animals were fed standard laboratory chow and water ad lib. Group 1 received no other treatment. Group 2 received a single injection of N-nitrosobis(2-oxopropyl)amine (BOP) (20 mg/kg sc), a dose known to produce pancreatic carcinomas within 28 wk. Group 3 had ethanol added to the drinking water (25% wt/vol) for the duration of the study, and received the same dose of BOP 2 wk after starting the ethanol treatment. After 24 wk, pancreatic juice was collected following secretin and cholecystokinin stimulation, and the pancreases were examined histologically by one of us who had no knowledge of the treatment regimen. The presence of ductal proliferation (Proliferative Index, PI) and neoplastic lesions (adenoma, carcinoma in situ, carcinoma) was recorded. The blood ethanol concentration was 130 +/-8 mg% in Group 3 animals. Chronic ethanol ingestion was associated with significantly less preneoplastic ductal proliferation and fewer neoplastic pancreatic lesions. The explanation for this observation is uncertain, but it may be related to ethanol's known ability to alter the metabolism of pancreatic secretory cells. Thus the carcinogen may have been metabolized differently in these animals. (no Refs)

87. INHIBITION OF PANCREATIC CARCINOGENESIS BY RETINOIDS IN AZASERINE-TREATED RATS.

Longnecker DS, Curphey TJ, Kuhlmann ET, Roebuck BD
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Cancer Res; 42(1):19-24 1982

Chemoprevention by retinoids of the progression of carcinomas induced in rats by azaserine was evaluated. Wistar/Lewis rats were given 15 weekly injections of azaserine, 10 mg/kg, while fed a chow diet; after the completion of carcinogen treatment, they were fed a chow diet supplemented with four different retinoids at the level of 0.5 to 2 mmol/kg diet for 1 yr. The incidence of neoplasms was determined by autopsy and histological study. The incidence of pancreatic carcinoma among a male positive control group (azaserine treated, but not retinoid treated) was 42%. The incidence of pancreatic carcinoma among male rats treated with retinoids was: N-2-hydroxyethylretinamide, 6%; N-4-propionyloxyphenylretinamide, 17%; and retinylidene dimedone, 12%. The incidence in rats fed these three retinoids was significantly (p less than 0.05) below the control group incidence. Thus, these three retinoids appeared to be effective in inhibiting the progression of pancreatic carcinomas in the azaserine-induced model. A similar trend was demonstrated in females, but statistical significance was shown only in rats fed N-2-hydroxyethylretinamide. A fourth retinoid, N-4-carboxyphenylretinamide, was more toxic and less effective in chemoprevention. Since retinoids were fed after exposure to carcinogen, the effect was exerted during the postinitiation phase of carcinogenesis. The ratio of invasive pancreatic carcinomas to localized carcinomas (carcinoma in situ) was clearly higher among non-retinoid-treated rats than among those treated with retinoids. This is consistent with retarded progression in the retinoid-treated groups. (Author abstract) (10 Refs)

88. PROMOTING EFFECT OF TESTOSTERONE PROPRIONATE ON EXPERIMENTAL EXOCRINE PANCREATIC TUMORS BY 4-HYDROXYAMINOQUINOLINE 1-OXIDE IN RATS.

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Toxicol Lett; 9(4):349-354 1981

The promotion of 4-hydroxyaminoquinoline 1-oxide (HAQO) induced pancreatic tumors by androgenic hormone was tested in male and female rats. Three male (1m, 2m, and 3m) and three female groups (1f, 2f, and 3f) each consisting of 20 rats received 9 mg/kg iv injection of HAQO. Groups 1m and 1f received no further treatment. All other groups were castrated and subsequently given weekly sc injections of 1 mg testosterone propionate (groups 3m and 3f) or 0.1 ml olive oil (groups 2m and 2f). At 400 days the rats were autopsied and representative samples of pancreatic tumors were examined by electron microscopy. Eight exocrine adenomas of the pancreas developed in group 1m; six exocrine tumors developed in group 3m. One exocrine insuloma pancreatic tumor developed in group 1f and five were observed in group 3f. No exocrine adenomas of the pancreas developed in the control group or in groups 2m or 2f. Apparently testosterone can promote the induction of pancreatic tumors in rats by HAQO. (9 Refs)

REVIEWS AND OTHER RELATED STUDIES

89. ETIOLOGY AND PREVENTION OF GASTRIC CANCER (MEETING ABSTRACT).

Stemmermann GN
No affiliation given
First UICC Conference on Cancer Prevention in Developing Countries, August 25-29, 1981, Nagoya, Japan. International Union Against Cancer 368 pp., 1981.

Three conditions have been identified as precursors to gastric cancer: Atrophic gastritis of the oxyntic mucosa, atrophic gastritis with intestinal metaplasia of the antral mucosa, and partial gastrectomy with gastroenterostomy. Mutagenic nitroso compounds have been identified in the gastric mucosa or gastric juice in each of these precursor states, and it is likely that these compounds are formed in the stomach itself. Identification of persons with these diseases is now possible, and this should identify asymptomatic persons who are most likely to benefit from a selective diagnostic screening program. The benefits of selective diagnostic screening for gastric cancer would probably be too few and too costly to justify its use in any but high risk areas, even when the cost of the procedure is minimized by the use of paramedical personnel. The use of vitamin C and E supplements to suppress endogenous nitrosation in high risk persons could be justified on theoretical grounds, but there is no hard evidence that this would lower the risk of gastric cancer. On a mass scale, however, it would be comparatively inexpensive and would do no harm. The potential benefits of vitamin supplements to large numbers of high risk persons need not be delayed since assessment of the efficacy of this form of intervention can be performed synchronously by following small, defined sub-groups of high risk persons. (no Refs)

90. MODIFICATION OF THE CARCINOGENIC PROCESS IN COLON CANCER BY ENDOGENOUS AND EXOGENOUS FACTORS (MEETING ABSTRACT).

Daugherty JP
University of Alabama School of Medicine, Birmingham, AL
International Symposium on Health Effects of Tumor Promotion, October 12-15, 1981, Cincinnati, Ohio US Environmental Protection Agency and the American College of Toxicology; 1981

The United States has one of the highest rates of colon cancer in the world, and the incidence and survival rates have changed little in the last 30 yr. There are several areas of responsibility in dealing with the health aspects of tumor promotion in colon carcinogenesis. The first of these involves an understanding of cancer epidemiology. Numerous epidemiological studies have implicated a variety of exogenous and endogenous factors in the etiology of human colon cancer. These factors have been demonstrated to influence numerous biochemical parameters by reacting with biomolecules, changing the transit time and vol of fecal material and altering intestinal microflora. The second area involves basic experimental investigations to determine the validity of the associations suggested by epidemiological findings. The development of screening methods for those individuals with a high risk for the development of colon cancer, as well as screening for potential carcinogens and modifiers of carcinogenesis is a third area of concern. A fourth area of concern is inhibition of the carcinogenic process. It is apparent that the best way to reduce the incidence of cancer is to prevent exposure to carcinogens. However, it is rarely possible to reduce or eliminate human exposure to cancer-causing agents, and it is necessary to approach cancer prevention by the use of agents which inhibit cancer formation. Since carcinogenesis is a prolonged, multistage process, a variety of approaches exist for inhibition of the carcinogenic process, either at the state of initiation, cocarcinogenesis or promotion. Finally, the possible role of therapeutic agents in the development of colon cancer should be examined especially in view of the alterations which these agents produce in the concentration and/or type of bile acid and cholesterol metabolites in the colon as well as alterations in various other agents. (no Refs)

☆ U.S. GOVERNMENT PRINTING OFFICE 1982—361-547/114

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1. NUTRITION AND ENVIRONMENTAL HEALTH: THE INFLUENCE OF NUTRITIONAL STATUS ON POLLUTANT TOXICITY AND CARCINOGENICITY. VOLUME 2: MINERALS AND MACRONUTRIENTS.

Calabrese EJ

Environmental Health Program, Div. Public Health, Univ. Massachusetts, Amherst, MA

Nutrition and Environmental Health: The Influence of Nutritional Status on Pollutant Toxicity and Carcinogenicity. Volume 2: Minerals and Macronutrients. New York, John Wiley and Sons, 468 pp., 1981.

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

2. RETROSPECT AND PROSPECT OF STUDIES ON DIGESTIVE SYSTEM DISEASES IN CHINA.

Zhang X

Dept. Internal Medicine, Capital Hosp., Chinese Acad. Medical Sciences, Beijing, People's Republic of China

Zhonghua Xiaohua Zazhi; 1(1):1-4 1981

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3. EPIDEMIOLOGY OF PITUITARY ADENOMAS.

Gold EB

Dept. Epidemiology, Sch. Hygiene and Public Health, Johns Hopkins Univ., 615 Wolfe St., Baltimore, MD, 21205

Epidemiol Rev; 3:163-183 1981

4. BLADDER CANCER EPIDEMIOLOGY.

Matanoski GM, Elliott EA

Dept. Epidemiology, Sch. Hygiene and Public Health, Johns Hopkins Univ., 615 North Wolfe St., Baltimore, MD, 21205

Epidemiol Rev; 3:203-229 1981

5. THE EPIDEMIOLOGY OF BENIGN BREAST DISEASE.

Ernster VL

Dept. Epidemiology and International Health, 1699HSW, Univ. California, San Francisco, CA, 94143

Epidemiol Rev; 3:184-202 1981

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN CARCINOGENESIS

6. AIR POLLUTION AND BIOLOGICAL DEFENCE.

Schlipkoter HW, Dolgner R

Med. Institut fur Umwelthygiene an der Univ., Gurlittstrasse 53, D-4000 Dusseldorf 1, W. Germany

Zentralbl Bakteriol [Orig A]; 172(4/5):299-311 1981

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7. CANCER AND THE PHYSICOCHEMICAL QUALITY OF DRINKING WATER IN QUEBEC.

Thouez JP, Beauchamp Y, Simard A

Dept. Geography, Univ. Montreal, Montreal, Quebec, Canada

Soc Sci Med [Med Geogr]; 15(1):213-223 1981

VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

8. ONCOGENIC VIRUSES.

Wyke JA

Imperial Cancer Res. Fund, P.O. Box 123, Lincoln's Inn Fields, London WC2A 3PX, England

J Pathol; 135(1):39-85 1981

9. ROLE OF VIRUSES IN THE ETIOLOGY OF NATURALLY OCCURRING FELINE LEUKEMIA.

Essex M, Grant CK, Cotter SM, Hardy Jr WD

Dept. Microbiology, Harvard Sch. Public Health, 665 Huntington Ave., Boston, MA [illegible]15

Haematol Blood Transfus; 26:4[illegible]-487 1981

METHODOLOGY IN CARCINOGENESIS RESEARCH

10. MAMMALIAN IN VIVO AND IN VITRO CYTOGENETIC ASAYS: A REPORT OF THE U.S. EPA'S GENE-TOX PROGRAM.

Preston RJ, Au W, Bender MA, Brewen JG, Carrano AV, Heddle JA, McFee AF, Wolff S, Wassom JS

Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN, 37830

Mutat Res; 87(2):143-188 1981

11. BACTERIAL SYSTEMS FOR CARCINOGENICITY TESTING.

Mohn GR

Dept. Radiation Genetics and Chemical Mutagenesis, State Univ. Leiden, Wassenaarseweg 72, 2333 AL Leiden, The Netherlands

Mutat Res; 87(2):191-210 1981

12. MUTAGENESIS BY CHEMICAL AGENTS IN V79 CHINESE HAMSTER CELLS: A REVIEW AND ANALYSIS OF THE LITERATURE.

Bradley MO, Bhuyan B, Francis MC, Langenbach R, Peterson A, Huberman E

Merck Inst. for Therapeutic Res., West Point, PA, 19486

Mutat Res; 87(2):81-142 1981

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13. CANCER BIOLOGY.

Ruddon RW

Biological Markers Program, NCI-Frederick Cancer Res. Center, Frederick, MD

Cancer Biology. New York, Oxford University Press, 344 pp., 1981.

14. AVOIDABLE CANCER: ATTRIBUTION OF RISK.

Doll R

Radcliffe Infirmary, Oxford, England

S Afr Cancer Bull; 25(3):125-146 1981

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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PREVALENCE OF GI CANCER IN HUMAN POPULATIONS

1. TRENDS IN THE ANATOMICAL DISTRIBUTION OF COLORECTAL CARCINOMA IN HAWAII, 1960-1978.

Nomura AM, Kolonel LN, Hinds MW

Epidemiology Program, Cancer Center Hawaii, Univ. Hawaii, 1236 Lauhala St., Honolulu, HI, 96813

Dig Dis Sci; 26(12):1116-1120 1981

The incidence of colorectal adenocarcinoma increased in the five major ethnic groups in Hawaii, but more in men than women. The highest rates were in the Chinese and Japanese. The site-specific time trend patterns revealed that the greatest increase occurred in rectosigmoid cancer, followed by cancer of the sigmoid colon and the transverse descending colon. Rectal cancer had minimal changes in rats over time. The comparison of site-specific rates between the Japanese in Hawaii and Miyagi Prefecture, Japan, showed that the occurrence of cancer of the rectosigmoid, sigmoid, and transverse descending colon was far greater in Hawaii than Miyagi with minimal differences in the rates of rectal cancer. The findings from this study indicate that the separate anatomical locations of colorectal cancer probably have some distinct etiologies that need further investigation. (Author abstract) (5 Refs)

2. MALIGNANT GASTRO-INTESTINAL TUMOURS. THE FREQUENCY DISTRIBUTION BY AGE, SEX, RACE AND SITE AT GROOTE SCHUUR HOSPITAL, CAPE TOWN, 1974-1978.

Dent DM, Vader CG

Dept. Surgery, Groote Schuur Hosp., Cape Town, South Africa

S Afr Med J; 60(23):883-885 1981

The observed frequency distribution of 2,023 primary malignant gastro-intestinal tumors recorded during the 5-yr period 1974-1978 is reported. The two most common sites were stomach (29.6%) and colon and rectum (29.5%), and the third most common was the esophagus (19.8%). Marked differences in the site of the tumors according to race were found; esophageal carcinoma was the most frequent lesion in Black patients (62.1%), gastric carcinoma in Colored patients (44.1%) and colorectal carcinoma in White patients (46.8%). Within the Black group rarely affected sites were the pancreas (5.1%) and colon and rectum (3.5%). (Author abstract) (6 Refs)

3. EPIDEMIOLOGY OF GASTRIC CANCER IN CHILE.

Armijo R, Detels R, Coulson AH

Div. Epidemiology, Public Health Sch., Univ. California, Los Angeles, CA

Bol Of Sanit Panam; 91(4):362-368 1981

After Japan, Chile has the highest gastric cancer mortality rate (GCM) in the world. GCM is lowest in northern and southern Chile (20/100,000) and highest in the middle region (Maule, 52.5/100,000). Levels of nitrates and nitrites have been studied in vegetables, saliva, and urine of children in different parts of Chile. (9 Refs) (In SPA)

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN GI CARCINOGENESIS

4. EPIDEMIOLOGIC STUDY OF DRINKING WATER CHLORINATION AND WISCONSIN FEMALE CANCER MORTALITY.

Young TB, Kanarek MS, Tsiatis AA

Dept. Preventive Medicine, Univ. Wisconsin, 504 North Walnut St., Madison, WI, 53706

JNCI; 67(6):1191-1198 1981

The association between gastrointestinal, urinary tract, brain, lung, and breast cancer mortality and drinking water trihalomethane exposure, as estimated by av daily chlorine dosage of water source 20 yr past, was investigated for Wisconsin white females by use of a death certificate-based case-control study design. A total of 8,029 cancer deaths and 8,029 controls (noncancer deaths) matched on county of residence, year of death, and age were taken from mortality records of 28 counties for the years 1972-77. Data on characteristics and treatment of municipal water supplied to the residences of cases and controls were obtained from questionnaires sent to the water superintendents of the 202 waterworks associated with the sample. By the use of logistic regression analysis, odds ratios for site-specific cancer death associated with high, medium, and low chlorine-dosed water as compared to unchlorinated water exposure were determined; the control variables were urbanicity, marital status, and occupation. With the exception of cancer of the colon, no anatomic cancer site was significantly associated with any chlorine dose exposure category. For colon cancer, odds ratios of 1.51 [95% confidence interval (CI) = 1.06-2.14], 1.53 (95% CI = 1.08-2.0) and 1.53 (95% CI = 1.11-2.11) were obtained for high-, medium-, and low-dose chlorination, respectively (p less than or equal to 0.02). For colon cancer cases and controls exposed to water sources affected by rural runoff, odds ratios of 3.30 (95% CI = 1.45-7.48), 3.60 (95% CI = 1.57-8.26), and 2.74 (95% CI = 1.10-6.88) were observed for high, medium, and low chlorine dosages 20 yr past (p less than 0.025). (Author abstract) (40 Refs)

DIETARY AND DIGESTIVE FACTORS IN GI CARCINOGENESIS

5. VITAMIN A STATUS AND ESOPHAGEAL CANCER RISK: EPIDEMIOLOGIC AND EXPERIMENTAL EVIDENCE FOR A POSITIVE ASSOCIATION.

van Rensburg SJ, Kruger EF, Louw ME, Du Plessis JP

Natl. Res. Inst. Nutritional Diseases, P. O. Box 70, Tygenberg 7505, South Africa

Nutr Rep Int; 24(6):1123-1131 1981

To evaluate the role of vitamin A in the etiology of esophageal cancer (EC), the occurrence of EC was studied in the Transkei territory (South Africa). A moderate incidence district (9.0/100,000) was used as a low risk region and a high incidence (50.5/ 100,000) district was used as the high risk region. The survey of the dietary intake and serum levels of vitamin A showed that deficient intake of vitamin A was 1-3x more common in the low risk groups. Elevated serum values were detected in 2-4 and 6-9 yr old children from high risk group. Experiments in BD IX rats showed that the incidence of methylbenzylnitrosamine-induced EC in animals who received a diet containing 30 mg/kg of vitamin A was 2x higher than that in the animals who received a diet containing 3 mg/kg of vitamin A. The rats who received vitamin A deficient diet were free of EC. (15 Refs)

6. THE LOW INCIDENCE OF COLORECTAL CANCER IN A 'HIGH-RISK' POPULATION: ITS CORRELATION WITH DIETARY HABITS.

Rozen P, Hellerstein SM, Horwitz C
Ichilov Hosp., Weizmann St., Tel Aviv, Israel
Cancer; 48(12):2692-2695 1981

In Israel, the incidence of colorectal cancer is highest in European-American-born Jews, although this incidence is lower than that found in European-born Jews living in the United States. A significantly lower-than-expected incidence was found in a specific kibbutz established by immigrants of European origin. Matched population samples from this kibbutz and the city of Tel Aviv revealed significant differences in dietary habits. The kibbutz members ate more unavailable carbohydrate and ascorbic acid and had a higher dietary polyunsaturated to saturated fat (P/S) ratio than the city dwellers. Both groups ate more crude fiber, less saturated fat, and less beef than has been reported from America and European countries. This kibbutz diet seems to have prevented large bowel cancer, parallels the 'prudent' diet of Wynder, and possibly indicates the feasibility of colorectal cancer prevention. (Author abstract) (34 Refs)

7. ESOPHAGEAL CANCER AMONG BLACK MEN IN WASHINGTON, D.C. II. ROLE OF NUTRITION.

Ziegler RG, Morris LE, Blot WJ, Pottern LM, Hoover R, Fraumeni JF
Environmental Epidemiology Branch, Div. Cancer Cause and Prevention, NCI, NIH, Public Health Service, U.S. Dept. Health and Human Services, Bethesda, MD, 20205
JNCI; 67(6):1199-1206 1981

A case-control study of esophageal cancer was conducted among the black male residents of Washington, D.C., to find reasons for the exceptionally high risk in this population. The next of kin of 120 esophageal cancer cases who died during 1975-1977 and of 250 D.C. black males who died of other causes were interviewed. Five indicators of general nutritional status - fresh or frozen meat and fish consumption, dairy product and egg consumption, fruit and vegetable consumption, relative wt (wt/ht(2)), and number of meals eaten per day - were each significantly and inversely correlated with the relative risk of esophageal cancer. Associations with other food groups were not apparent. The least nourished third of the study population, defined by any of these five measures, was at twice the risk of the most nourished third. None of these associations was markedly reduced by controlling for ethanol consumption, the other major risk factor in this population; smoking; socioeconomic status; or the other nutrition measures. When the three food group consumption measures were combined into a single overall index of general nutritional status, the relative risk of esophageal cancer between extremes was 14. Estimates of the intake of vitamin A, carotene, vitamin C, thiamine, and riboflavin were inversely associated with relative risk; but each micronutrient index was less strongly associated with risk than were the broad food groups that provide most of the micronutrient. Thus no specific micronutrient deficiency was identified. Instead, generally poor nutrition was the major dietary predictor of risk and may partially explain the susceptibility of urban black men to esophageal cancer. (Author abstract) (31 Refs)

8. N-NITROSO COMPOUNDS: DIET AND CANCER TRENDS; AN APPROACH TO THE PREVENTION OF GASTRIC CANCER.

Weisburger JH
American Health Foundation, Valhalla, NY, 10595
ACS Symp Ser; 174():305-317 1981

Documented evidence for human cases of cancer unambiguously associated with short chain dialkylnitrosamines detected in foods in the Western world has not been presented yet. Other high risk regions have in common low intakes of foods with vitamin C. The risk factors for human gastric cancer include foods pickled with salt and saltpeter or residence in areas with high geochemical nitrate. Mutagenic activity was found for Salmonella typhimurium TA 1535 with an extract of a pickled fish frequently eaten in high risk Japan, which also induced glandular stomach cancer in rats. The formation of the mutagen can be blocked by vitamin C. In the control group (8 rats) fish extract alone was given, and no neoplastic changes in the stomach or pancreas were seen. Twelve rats were administered with extract of nitrite-treated fish. Glandular hyperplasia (6/12), squamous cell hyperplasia of the forestomach epithelium (5/12), and intestinal metaplasia was noted in this group. Several other neoplasias were noted in this group. Formation of nitrosoureido derivative can be blocked by vitamin C, vitamin E, and some other substances such as gallates. (66 Refs)

9. NUTRITIONAL ASPECTS OF CANCER PREVENTION: AN OVERVIEW.

Silverman J
American Health Foundation, Naylor Dana Inst Disease Prevention, Valhalla, NY, 10595
J Am Vet Med Assoc; 179(12):1404-1409 1981

Human epidemiologic studies and supporting laboratory animal data on the relationship between nutrition and modification of cancer are reviewed. Carcinogenesis results from at least two steps: initiation and promotion. Diet, a major risk factor, can influence cancer in several ways. Food additives or contaminants can act as initiators, promoters, or inhibitors; nutritional deficiencies can cause biochemical changes. Nutritional excesses can cause metabolic changes which may then promote or inhibit cancer. A decrease in caloric intake leads to an increase in tumor latency and a decrease in the number of tumors. The incidence of breast cancer in humans is positively correlated with the consumption of animal protein, fat, and simple carbohydrates. Dietary fat also exerts a promotional effect on colonic cancer. Cancer of the prostate and pancreas is positively correlated with fat consumption, but the evidence is not absolute. Vitamin A apparently inhibits tumor formation during the promotional phase. Vitamin C does not manifest a clear protective effect against any cancer. Studies with selenium have produced disparate results, while nitrosamines have shown carcinogenicity in many species. In most cases nutrients modify rather than cause cancer. (100 Refs)

10. NUTRIENT INTAKES AMONG RURAL TRANSKEIANS AT RISK FOR OESOPHAGEAL CANCER.

Groenewald G, Langenhoven ML, Beyers MJ, Du Plessis JP, Ferreira JJ, Van Rensburg SJ
(c/o van Rensburg), Natl. Res. Inst. Nutritional Diseases, P.O. Box 70, Tygerberg 7505, South Africa
S Afr Med J; 60(25):964-967 1981

The frequency of low nutrient intakes was investigated in areas of moderate and high esophageal cancer incidence in Transkei by means of 24-hr recall and habitual intake studies in children and nursing mothers. The results in moderate- and high-risk regions were similar and habitual intakes of protein, energy, phosphorus, iron, thiamine and vitamin A were generally satisfactory. Intakes of less than two-thirds the Recommended Dietary Allowances (RDA) had a high frequency of inadequate intakes for calcium (90%), nicotinic acid (79%), riboflavin (55%) and ascorbic acid (50%). It is concluded that the possibility of long-standing deficiencies of the latter three vitamins playing a role in esophageal carcinogenesis should be considered. (Author abstract) (13 Refs)

OTHER ETIOLOGIC FACTORS IN GI CARCINOGENESIS

11. PRIMARY CANCER OF THE GASTRIC STUMP: COMMENTS ON 18 CASES.

Abrao A, Possik RA, Cappellano RS, Do Amarante AP
Departamento de Cirurgia Abdominal, Hospital A. C. Camargo, Sao Paulo, Brazil
Rev Paul Med; 97(7/9):116-120 1981

Eighteen patients (52-78 yr old, 15 males and 3 females) with primary cancer of gastric stump (GS) confirmed by histologic examination were studied. Time interval between surgery for gastric ulcer and diagnosis of GS cancer was 11-30 yr. Frequency of GS cancer went from 1 in 1962-1965 to 10 in 1974-1977, while the total number of gastric cancer has not changed to much (365 to 378), probably due to the fact that gastrectomy was performed in larger numbers starting from 1950. Thirteen adenocarcinomas (AC), 3 undifferentiated AC, 1 papilliferous AC and 1 mucinous AC were diagnosed by histopathology. In one case GS tumor was located next to the anastomosis, which had a papilliferous aspect and a histopathologic diagnosis of papilloma. This indicates an intermediary stage in malignant degeneration. Ulcers occured in mucosa on the jejunal and duodenal side of anastomoses. Ulcerated lesions of intestinal mucosa were also of peptic nature. Of the 18 patients 4 were inoperable, 3 had exploratory laparotomy and 11 surgery. Two patients died after surgery, three others 1-15 mo later, 1 was asymptomatic, but committed suicide 6 mo after surgery and 1 patient was living without symptoms 24 mo later. Lymph node involvement (LNI) was seen in 17 patients, and 1 patient without LNI committed suicide. (22 Refs) (In POR)

12. SERUM CHOLESTEROL AND COLON CANCER INCIDENCE IN HAWAIIAN JAPANESE MEN.

Stemmermann GN, Nomura AM, Heilbrun LK, Poliack ES, Kagan A
Kuakini Medical Center, 347 North Kuakini St., Honolulu, HI, 96817
JNCI; 67(6):1179-1182 1981

A prospective study of cancer and coronary heart disease (CHD) in 8,006 Hawaiian Japanese men, aged 45-68 yr, showed that serum cholesterol levels below 180 mg/dl predicted low rates of CHD and high rates of colon cancer. Men with colon cancer had lower mean serum cholesterol levels than did other members of the cohort, including those with cancer at other sites. The lowest serum cholesterol levels were obtained from men who died as a result of colon cancer. The lack of such an association with other cancers and the persistence of this inverse association in colon cancer patients diagnosed 5-9.9 yr after examination suggest that the low serum cholesterol was not due to preexisting disease. Right colon tumors showed the strongest inverse association with serum cholesterol. The differences between CHD and colon cancer in respect to serum cholesterol indicate that different subsets of the westernized Japanese population are affected. (Author abstract) (12 Refs)

13. A COMPARISON OF CANCER RISK IN CROHN'S DISEASE AND ULCERATIVE COLITIS.

Greenstein AJ, Sachar DB, Smith H, Janowitz HD, Aufses AH
Dept. Surgery, Mount Sinai Medical Center, One Gustave L. Levy Place, New York, NY, 10029
Cancer; 48(12):2742-2745 1981

The authors estimated cancer risk among 579 patients hospitalized with Crohn's disease between 1960-1976 by calculating the ratios of observed number of cancers (O) in our hospital sample to the expected number of cancers (E) based on the age- and sex-specific cancer rates of a standard population. The authors then compared these O/E ratios with the O/E ratios similarly calculated among 267 patients hospitalized with ulcerative colitis. The risk of colorectal cancer was significantly increased in Crohn's disease (O/E = 6.9, p less than 0.001). This increase was similar in magnitude to that found in left-sided ulcerative colitis (O/E = 8.6, p less than 0.001) but was much less than that found in universal ulcerative colitis (O/E = 26.5, p less than 0.001). The incidence of small bowel cancer was greatly increased in the combined group of regional enteritis and ileocolitis (O/E = 85.8, p less than 0.001), and even more so in the regional enteritis group alone (O/E = 114.5, p less than 0.001). The incidence of extraintestinal cancer did not increase in any of the patient groups. (Author abstract) (23 Refs)

14. ADENOCARCINOMA IN PERINEAL FISTULAS OF CROHN'S DISEASE.

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Dis Colon Rectum; 24(8):639-643 1981

Until recently, Crohn's disease has not been regarded as a premalignant lesion, but the increasing number of patients with Crohn's disease in whom adenocarcinoma of the gastrointestinal tract develops strongly suggests that these patients are indeed at a higher risk for carcinoma. These patients are usually young and tend to develop a malignancy in the bypassed ileum or right colon. Patients with such lesions usually have poor prognosis. Adenocarcinoma arising in perineal fistulas secondary to Crohn's disease has not been reported in English medical literature except for one case published in 1975. In this article, the authors report a second, similar case of Crohn's disease with recurrent perineal fistulas. An infiltrating adenocarcinoma developed in these fistulas, in the anorectal region, and in the left labia. The risk of malignancy should be seriously considered in the management of Crohn's disease, especially in young patients. Because of the risk of adenocarcinoma in these patients, resection rather than bypass is recommended in the surgical management. (Author abstract) (14 Refs)

INDUCTION OF GI CARCINOGENESIS IN ANIMALS

15. GASTRIC ULCERS AND PRODUCTION OF GASTRIC CARCINOMA IN DOGS AND RATS: GASTRIC CARCINOMA INDUCED BY N-METHYL-N'-NITRO-N-NITROSOGUANIDINE (MNNG) OR N-ETHYL-N'-NITRO-N-NITROSOGUANIDINE (ENNG) (MEETING ABSTRACT).

Koyama Y, Ohmori K, Maruyama K, Hirota T, Ushio K
Dept. Surgery, Natl. Cancer Center Hosp., Chuo-ku, Tokyo 104, Japan
Program and Abstracts of the 37th Meeting of Japanese Research Society for Gastric Cancer in Tokyo, 3 July, 1981. Japanese Research Society for Gastric Cancer, Tokyo 113, Japan, 6, 1981.

In the first experiment, nine beagles in which ulcers were produced in the stomach by electric cautery were given drinking water containing 50 ug of N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) per ml for 10 mo, and autopsies were performed 12-64 mo later. Six gastric carcinomas were produced in the nine beagles. Three of the carcinomas (2 signet ring cell carcinomas and 1 differentiated carcinoma) were formed at the artificial ulcerative scar. There were two carcinomas without ulcers (signet ring cell carcinoma and differentiated carcinoma) and one carcinoma with an ulcer which was not artificial. In the second experiment, after two beagles were given a 0.1% indoacetamide (IAM) soln for 3 mo, they were given food soaked in a 150 ug of N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG) per ml soln and IAM for 10 mo. A diffuse erosive change occurred in the beagles which were given IAM singly, but the change was enhanced by the addition of ENNG, and carcinoma developed after 12-13 mo and the beagles died within 2 yr. Little erosive change occurred in the beagles which were given ENNG singly and microcarcinoma appeared 9-20 mo later. In the third experiment, an ulcer produced by cautery or by IAM was also the most common site of the MNNG-in duced gastric carcinoma in Wistar rats. Therefore, an ulcerative lesion is considered to be the site of action of the carcinogenic factor. (no Refs) (In JPN)

16. CANINE SCIRRHOUS GASTRIC CARCINOMA (MEETING ABSTRACT).

Miyasaka K, Kurihara M, Izumi T, Maruyama T, Sasaki Y, Yamatani F, Shirakabe H, Kamano T, Yasui A
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Program and Abstracts of the 37th Meeting of Japanese Research Society for Gastric Cancer in Tokyo, 3 July, 1981. Japanese Research Society for Gastric Cancer, Tokyo 113, Japan, 6, 1981.

Ten dogs were divided into three groups as follows: Group 1 (4 dogs), po administration of N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG) (in food soaked with ENNG) for the first 4 mo and ENNG administration combined with sc injection of 5-10 gamma of gastrin per kg for the next 4 mo; Group 2 (3 dogs), administration of ENNG for 1 yr, but combined with sc injection of 5-10 gamma of gastrin per kg for 2 mo from the 5th mo of the administration of ENNG and for 6 mo from the 2nd mo from the end of the administration of ENNG; Group 3 (3 dogs), sc injection of 5-10 gamma of gastrin per kg for 7 mo after po administration of ENNG for 8 mo and then administration of serotonin for 8 mo. Scirrhous carcinoma with wall hypertrophy and stenosis on the pyloric antrum developed in one dog per group (a total of 3 dogs). The scirrhous carcinoma was histologically poor differentiated adenocarcinoma. Mucinous cells were observed in part of the carcinoma and infiltration into the serosa accompanied by marked proliferation of collagenic fibers was seen. It is suggested that the production of scirrhous gastric carcinoma involves gastrin. (no Refs) (In JPN)

17. A STUDY ON CARCINOGENESIS INDUCED BY DEGRADED CARRAGEENAN ARISING FROM SQUAMOUS METAPLASIA OF THE RAT COLORECTUM.

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Cancer Lett; 14(3):267-272 1981

Carcinogenesis in the colorectum of F344 rats fed diets containing 10% degraded carageenan for varying lengths of time was investigated. After termination of carageenan administration, all rats were fed a basal diet until sacrifice 18 mo after initial administration. In males treated for 2 mo, the incidence of colorectal squamous metaplasia was 100%, with tumors in 5/39 animals. The tumors were squamous cell carcinoma, anaplastic carcinoma, and adenoma. In males treated for 6 mo, metaplasia was evident in 100% and 8/42 rats had tumors. In males treated for 9 mo, 100% of animals showed squamous metaplasia and 17/42 had tumors. No inflammatory or neoplastic changes were found in control animals. (10 Refs)

18. LACK OF CARCINOGENICITY IN MICE OF 4,4'-DIAMINOBENZANILIDE AND 4,4'-DIAMINOAZOBENZENE, TWO INTERMEDIATES USED IN THE MANUFACTURE OF AZO DYES.

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Cancer Lett; 14(3):329-336 1981

A long-term bioassay for carcinogenicity of 4,4'-diaminobenzanilide (DABA) and 4,4'-diaminoazobenzene (DAAB) was conducted in BALB/c mice. Male and female mice received DABA or DAAB in the diet (100, 300, or 600 ppm) beginning at 8 wk of age and continuing for 60 wk. Animals were then returned to a normal diet and observed for an additional 50 wk. No differences were seen between any of the treated groups and controls. No association was observed between treatment and incidence of any particular tumor with the exception of adrenal cortex tumors, which were seen at lower incidence in DAAB-treated males. Malignant lymphomas originated most frequently in the spleen, mesenteric lymph nodes, and Peyer's patches, and were seen more frequently in females but not in excess of control values. Liver cell tumors occurred with very low frequency. (15 Refs)

MECHANISMS AND MODIFICATIONS OF GI CARCINOGENESIS

19. EFFECT OF SEX HORMONES ON PRODUCTION OF GASTRIC CARCINOMA (MEETING ABSTRACT).

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Program and Abstracts of the 37th Meeting of Japanese Research Society for Gastric Cancer in Tokyo, 3 July, 1981. Japanese Research Society for Gastric Cancer, Tokyo 113, Japan, 6, 1981.

To determine whether or not sex hormones are related to carcinogenicity which differs in males and females, the following experiment was performed. Wistar rats were divided into four groups: Group 1, administration of 50 ug of N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) per ml for 4 mo to male rats; Group 2, administration of 50 ug of MNNG per ml for 2 mo and subsequent sc injection of 400 ug of 17beta-estradiol (E2) per kg once a wk for 4 mo to male rats; Group 3, administration of 50 ug of MNNG per ml for 4 mo after male rats received orchiectomy; Group 4, administration of 50 ug of MNNG per ml for 4 mo to female rats. The rats were killed and examined 12 mo later. The incidence of gastric carcinoma after 12 mo from the beginning of the experiment in Groups 1, 2, 3 and 4 was 88%, 68%, 29% and 0%, respectively. Therefore, it was concluded that the injection of E2 and orchiectomy inhibited carcinogenesis. Rats in Groups 1, 2 and 4 were killed at the 4th, 6th, 8th and 10th mo. In Group 1, the incidence of carcinoma was 9%, 10%, 40% and 57% at the 4th, 6th, 8th and 10th mo, respectively: ie, the incidence of carcinoma increased with time. In Group 2, the incidence of carcinoma was lower than in Group 1, but the same tendency as in Group 1 was observed. In Group 4, hardly any carcinoma was observed. Changes in the gastric mucosa by erosion in the early stage in these three groups occurred in parallel with the incidence of gastric carcinoma at a high rate. Therefore, sex hormones are considered to have an effect on the incidence of carcinoma from the early stage. (no Refs) (In JPN)

20. CYTOTOXIC EFFECTS AND METABOLISM OF BENZO[A]PYRENE AND 7,12-DIMETHYLBENZ[A]ANTHRACENE IN DUODENAL AND ILEAL EPITHELIAL CELL CULTURES.

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JNCI; 67(6):1353-1362 1981

Two epithelial cell lines have been established from the duodenum (IEC-17) and the ileum (IEC-18) of outbred germ-free Crl:CD(SD)GN rats. They have a very similar morphology and ultrastructure, a normal rat diploid karyotype, comparable growth rates, and a similar set of surface antigens as detected with monoclonal antibodies specific for intestinal epithelial cell surface proteins in vivo. Both cell lines do not grow in soft agar and when injected into syngeneic animals do not form tumors. The toxic effects of benzo[a]pyrene (BP) and 7,12-dimethylbenz[a]anthracene (DMBA) were studied in these two cell lines. The IEC-18 cells were found to be much more sensitive to both chemicals than the IEC-17 cells. In particular, at concentrations greater than 1 ug/ml, DMBA completely and irreversibly inhibited cell proliferation in the IEC-18 cells, whereas it produced a less marked and reversible inhibition in the IEC-17 cells. The metabolism of BP and DMBA to water-soluble products was studied; BP was apparently metabolized at similar rates in the two cell lines, whereas a striking difference was observed with DMBA, which was metabolized at a rate 10-15x greater in the IEC-18 cells than that in the IEC-17 cells. These results suggest that cultured cell lines derived from different portions of the intestinal tract have similar properties in vitro, but they may have very different responses to chemical carcinogens. (Author abstract) (34 Refs)

21. EFFECT OF RETINOIDS ON THE INDUCTION OF COLON CANCER IN F344 RATS BY N-METHYL-N-NITROSOUREA OR BY 1,2-DIMETHYLHYDRAZINE.

Silverman J, Katayama S, Zelenakas K, Lauber J, Musser TK, Reddy M, Levenstein MJ, Weisburger JH
American Health Foundation, Naylor Dana Inst. Disease Prevention, Valhalla, NY, 10595
Carcinogenesis; 2(11):1167-1172 1981

The possible modifying effect of synthetic and natural retinoids on the incidence of colon cancer in rats induced by two intrarectal doses of 2.5 mg of N-methyl-N-nitrosourea (MNU) given once a wk for 2 successive wk or a single 150 mg/kg body weight dose of 1,2-dimethylhydrazine (DMH), sc was investigated. Emphasis was on the effect of the development of early tumors as visualized by endoscopy. With the retinoids N-ethyl-retinamide, N-2-hydroxyethylretinamide, N-(4-hydroxyphenyl)-all-trans-re tinamide (RAHA) and retinyl acetate (RA) administered orally after the carcinogens, significant differences in early developing tumors were not found. At histopathological examination of the tumors the RAHA + DMH group had significantly fewer adenomas per animal. The percentage of adenoma bearing rats was significantly lower in groups receiving RAHA + DMH or RA + DMH. However, food consumption was lower in rats consuming either RAHA or RA Retinyl palmitate (RP) and RAHA were administered intrarectally to MNU-induced rats either before or after the carcinogen. When administered before MNU, RP caused a significant increase in the percentage of tumor bearing animals and the av number of tumors per animal as visualized endoscopically. At histopathological examination, all retinoid groups except RAHA given after the carcinogen, produced significantly more adenomas per animal and a significantly greater adenoma incidence than did the control groups. Thus, in two systems, the oral administration of retinoids did not clearly inhibit the early or later stages of colon tumor development. Intrarectal infusion of two retinoids had no effect on colonic morphology but at histopathological examination of later stage tumors there was an enhanced adenoma response. (Author abstract) (36 Refs)

22. EFFECTS OF THREE RETINOIDS ON COLON ADENOCARCINOMAS, SARCOMAS AND HYPERPLASTIC POLYPS INDUCED BY INTRARECTAL N-METHYL-N-NITROSOUREA ADMINISTRATION IN MALE F344 RATS.

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Microbiological Assoc., Inc., 5221 River Road, Bethesda, MD, 20816
Carcinogenesis; 2(11):1161-1166 1981

Male F344 rats, 9 wk of age, were given multiple intrarectal administrations of N-methyl-N-nitrosourea (NMU) at 0.5 mg/dose twice a wk for a total of 8, 12, or 16 doses. Five days after the final NMU instillation, rats were placed on one of four diets; chow with retinoid vehicle, chow with 654 mg N-ethylretinamide per kg diet, chow with 686 mg N-(2-hydroxethyl)retinamide per kg diet, or 406 mg retinylidene dimedone per kg diet. Groups of 40-50 rats receiving 16, 12, or 8 total doses were sacrificed 32, 44, or 52 wk after the initial NMU dose, respectively. The number of rats with colon tumors and the number of tumors per tumor bearing rat in each dosage regimen was compared to appropriate controls. Organ weights for testis, liver, and kidneys were similar for controls and retinoid treated animals and no histopathologic lesions indicative of retinoid toxicity were found. Unusual proliferative lesions of the colon in rats of all dosed groups included hyperplastic and inflammatory polyps and sarcomas. The feeding of diets containing these three retinoids did not significantly modify the incidence or multiplicity of colon tumors observed under these conditions. (Author abstract) (18 Refs)

23. CHEMICAL PROTECTION AGAINST GASTROINTESTINAL RADIATION INJURY IN MICE BY WR-2822 , WR-2823, OR WR-109342 AFTER 4 MEV X-RAY OR FISSION NEUTRON IRRADIATION (MEETING ABSTRACT).

Connor AM, Sigdestad CP
Therapeutic Radiology Department, University of Louisville School of Medicine, Louisville, KY, 40292
Conference on Chemical Modification: Radiation and Cytotoxic Drugs, September 17-20, 1981, Key Biscayne, Florida. Committee for Radiation Oncology Studies 139 pp., 1981.

Three compounds were tested for their radioprotective properties against the effects of 4 MeV x-rays or fission neutron irradiation. The endpoints tested were lethality, intestinal crypt survival, and DNA synthesizing cellularity. Two of the compounds tested; S-2(4-aminobutylamino)ethylphosphorothioic acid (WR-2822) and the aminopentylamino derivative (WR-2823) are closely related to WR-2721. The third agent was the iminothiol derivative of 1-methylaminoadamantine (WR-109342). All drugs were administered via ip injections at their approximate max tolerated dose. WR-2822 was shown to have a slight protective effect against x-rays and neutrons. The dose modification factor (DMF) for gastrointestinal death (LD50/6) was 1.23 for x-rays and 1.51 for neutrons. The assay for intestinal crypt survival produced DMF's of 1.44 (x-rays) and 1.4 (neutrons). WR-2823 also showed a protective action in these assays. The DMF of LD50/6 was 1.32 for x-rays and 1.21 for neutrons. The respective DMF's for crypt survival were 1.23 (x-rays) and 1.42 (neutrons). WR-109342 was found to be extremely toxic and had no significant protective effects. All three drugs were more toxic and demonstrated less protection in most of these assays then the benchmark radioprotective agent WR-2721, although WR-2822 protected against the lethal effects of fission neutrons almost as well as WR-2721. Both WR-2822 and WR-2823 produced greater protection in the crypt survival assays for fission neutron irradiation than WR-2721. (no Refs)

BIOCHEMICAL, MORPHOLOGICAL AND IMMUNOLOGICAL ASPECTS OF GI CARCINOGENESIS

24. EXPERIMENTAL STUDY ON LYMPHATIC VASCULAR CHANGES IN THE DEVELOPMENT OF CANCER.

Tanigawa N, Kanazawa T, Satomura K, Hikasa Y, Hashida M, Muranishi S, Sezaki H
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Lymphology; 14(4):149-154 1981

Sudan Black B and Sudan Blue can partly enter the lymphatics of the small intestine from the lumen with long chain fatty acids. By use of a fat emulsion saturated with them, small intestinal and mesenteric lymphatics were clearly delineated. Subserosal and mesenteric lymphatics of the small intestine appeared as blue lines. With this method we studied anatomical changes of the lymphatic vessels during the development of cancer. An experimental tumor VX2 carcinoma was used. Lymphatic vessels were not found in cancerous regions by this lymphangiographic procedure, even in the early stages of cancer. Lymphatics pass ing through the tumorous tissue were completely obstructed and accompanied with peripheral dilatation. Compared to the morphological changes of the blood vessels, which were studied microangiographically, the lymphatic vessels were more easily affected by the malignant growth. (Author abstract) (11 Refs)

25. LDH ISOENZYME PATTERNS IN TUMORS, POLYPS, AND UNINVOLVED MUCOSA OF HUMAN CANCEROUS COLON.

Carda-Abella P, Perez-Cuadrado S, Lara-Baruque S, Gil-Grande L, Nunez-Puertas A

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Cancer; 49(1):80-83 1982

By using a method of electrophoresis separation, the authors determined the relative values of each one of the lactic dehydrogenase (LDH) isoenzymes in the normal colonic mucosa. In adenocarcinomas, there is a significant rise in the percent of LDH-5. A similar disturbance has been demonstrated in 14 polyps, which confirms the known precancerous condition of these lesions. In the uninvolved mucosa surrounding neoplasm, the authors found that the increase in the relative proportion of 'type M' isoenzymes, starting at 2 cm from the edge of the tumor, progressively disappears as the samples are taken farther away from the neoplasm. The authors conclude that these LDH isoenzyme pattern shifts in a normal mucosa could be an early sign of malignancy before the morphologic changes and could also be of great interest in the prediction of cancer relapse in the suture line after surgery. (Author abstract) (10 Refs)

26. A COMPARATIVE ULTRASTRUCTURAL STUDY OF HYPERPLASTIC AND ADENOMATOUS POLYPS, INCIDENTAL AND IN ASSOCIATION WITH COLORECTAL CANCER.

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Cancer; 48(12):2746-2755 1981

Adenomatous polyps of the colon were examined by light and electron microscopy in high risk patients having synchronous carcinoma and in low risk patients having incidental polyps only. There was no difference between these groups when polyp size, degree of dysplasia, and pattern of growth were correlated at light microscopic level. However, the groups differed ultrastructurally; the synchronous polyps showed atypical features, characterized in particular by abnormal secretory droplets and increased numbers of undifferentiated cells. Hyperplastic polyps were also included in the study and showed no atypia. Previously, adenomas from cases of familial polyposis coli have been shown to contain similar abnormal secretory droplets, and it is suggested that this ultrastructural change may be an important marker of early malignancy. Histochemistry and immunohistology may help to characterize the secretory material further. (Author abstract) (26 Refs)

27. HISTOAUTORADIOGRAPHIC STUDY OF GASTRIC EPITHELIAL DNA SYNTHESIS IN PRECANCEROUS LESIONS OF THE STOMACH.

Sizikov AI, Azykbekov R
Kirghiz Res. Inst. of Oncology and Radiology, Frunze, USSR
Vopr Onkol; 27(10):19-22 1981

Histoautoradiographic procedures were employed to establish the level of cell proliferation in gastric epithelium, using biopsy material from 84 patients: 59 cases suffering from gastritis (superficial 10, glandular lesions other than atrophy 18, mild atrophy 13, moderate atrophy 11, severe atrophy 7), 17 cases of peptic ulcer and 8 patients with adenomatous polyposis. Cell proliferation level in patients with peptic ulcer and polyps was identical to those in cases of non-atrophic gastritis or mild atrophy of mucosa. In cases of gastritis, the rise in cell proliferation is matched by the advancement of atrophic changes and reaches its peak in patients with severe atrophic gastritis. It is suggested that chronic gastritis involving pronounced atrophy of mucosa constitutes the most important factor of risk of cancer among the other precancerous lesions of the stomach. (Author abstract) (7 Refs) (In RUS)

28. THE IMMUNE RESPONSE TO CARCINOMA OF THE COLON IN A RAT MODEL: A TEMPORAL STUDY.

House AK
Queen Elizabeth II Medical Center, Nedlands 6009, Western Australia
Aust NZ J Surg; 51(5):487-493 1981

Carcinoma of the colon was induced in rats by treatment with 1,2-dimethylhydrazine (DMH). Macroscopic tumors were observed from 8 wk after commencing DMH injections and rapidly increased in mass to cause death of the animals between 20 and 27 wk later. Tumor immunity was assessed by the gross parameters of body, spleen and mesenteric lymph node weight and by in vitro tests of lymphocyte antitumor cytotoxicity and leukocyte migration inhibition by tumor and normal colon homogenates. Immune responses were recorded in control (saline treated) and in tumor (DMH treated) rats. Body wt of the tumor rats paralleled that of control animals until tumors were well advanced. At this time tumor animal body wt was significantly less than that of control animals. Spleen wt and in vitro lymphocyte antitumor cytotoxicity were significantly greater in tumor than in control rats and were so found soon after macroscopic tumors were observed. Mesenteric lymph node wt and leukocyte migration inhibition did not change until late in tumor development, but at this time there was an immune response in tumor animals. The study showed that carcinoma of the colon induced in rats was associated with an antitumor immune response and that this change occurred soon after macroscopic tumors were present. In spite of this the animals died of their neoplasms. (Author abstract) (27 Refs)

PANCREATIC CARCINOGENESIS

29. ENHANCEMENT OF EXPERIMENTAL PANCREATIC CANCER IN SYRIAN GOLDEN HAMSTERS BY DIETARY FAT.

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JNCI; 67(6):1327-1332 1981

The effects of dietary fat on the induction and development of pancreatic ductular adenocarcinoma were studied in random-bred Syrian golden hamsters. Diets containing low-fat (LF) or high-fat (HF) levels of corn oil [4.5 or 18.0 g/385 kilocalorie (kcal)], contributing 10 or 41% of the cal, respectively, were fed either before or after a single injection of N-nitrosobis(2-oxopropyl)amine (BOP) (10 mg/kg body wt). Control hamsters were fed corn oil at a medium-fat (MF) level (9 g/385 kcal) for life. The incidence of ductular adenocarcinomas increased in both males and females (LF diet, 16%; HF diet, 34%) when the HF diet was fed after BOP treatment. The av number of carcinomas per carcinoma-bearing animal also increased (LF diet, 1.3; HF diet, 3.0), but the carcinoma incidence was not influenced by these diets being fed before carcinogen treatment. The incidence of ductular adenomas was high with all treatments and was not influenced by diet. However, the number of adenomas was increased in animals fed HF diets. In addition, the incidence of acinar cell nodules was elevated in animals fed the MF and HF diets after BOP administration. These results showed that dietary fat modified the development of experimental ductular adenocarcinoma of the pancreas. (Author abstract) (31 Refs)

REVIEWS AND OTHER RELATED STUDIES

30. THE MICROECOLOGY OF GASTRIC CANCER.

Correa P, Tannenbaum SR
Dept. Pathology, Louisiana State Univ. Medical Center, New Orleans, LA, 70112
ACS Symp Ser; 174():319-329 1981

Evidence supporting the proposition that the etiologic factors of stomach cancer, operate by modifying the microenvironment of the gastric mucosa is reviewed. The progressive histological lesions of the mucosa, the altered gastric secretions, and the dietary items which apparently have an overriding influence in the gastric carcinogenesis are discussed. Observations indicate that the disease is determined mostly by the environment and not by the race of the population. The populations migrating from a high-risk area to a low-risk area keep their original high risk in the host country. The process of cancerization in the stomach mucosa seems to be a continuum of changes which turns a normal cell into a metaplastic cell and then to a progressively dysplastic cell and finally a cancerous cell. The hydrogen ion concentration (pH) and alterations in other gastric secretions (pepsinogens, blood group substances) take place in chronic atrophic gastritis. The microecology of the junction areas with high and low pH provides the unusual circumstances of having nitrate, nitrite, abundant bacteria, and a wide range of pH. High nitrite levels in the gastric cavity have been associated with the acceleration of the gastric cancer induction in experimental animals. (33 Refs)

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Farber E
Dept. Pathology, Univ. Toronto, 100 College St., Toronto, ON M5G 1L5, Canada
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Harevaenget 44, DK-4200 Slagelse, Denmark
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Ioannides C, Delaforge M, Parke DV
Dept. Biochemistry, Univ. Surrey, Guildford, Surrey GU2 5XH, England
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4. CARCINOGENIC, MUTAGENIC, TERATOGENIC WORKSHOP.
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Dept. Radiation Medicine, Massachusetts General Hosp., Boston, MA, 02114
Cancer Clin Trials; 4(Suppl):37-41 1981

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Sinclair WK, Failla P, Bond VP, Loewe WE, Kerr GD, Auxier J, Wyckoff OH, Maruyama T, Schull JW, Land EC, Dobson LR, Mays WC, Seymour J
Argonne Natl. Lab., 9700 South Cass Ave., Argonne, IL, 60439
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Institut fur Sozial- und Praventivmedizin, Universitat Zurich, Gloriastrasse 32 B, 8006 Zurich, Switzerland
Praxis; 70(43):1903-1912 1981
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Horowitz RM
U. S. Dept. Agriculture, Agricultural Res. Service, Fruit and Vegetable Chemistry Lab., Pasadena, CA, 91106
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8. ETIOLOGICAL CONCEPTS IN CERVICAL CARCINOGENESIS.
Kessler II
Dept. Epidemiology and Preventive Medicine, Univ. Maryland Sch. Medicine, 655 West Baltimore St., Baltimore, MD, 21201
Gynecol Oncol; 12(2,part2):S7-S24 1981

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Torres A, Martinez Guibelalde F, Gomez Garcia P, Garcia Castellano JM, Manzanares Escribano MR
Jefe Servicio Hematologia, Ciudad Sanitaria 'Reina Sofia' de la Seguridad Social, Cordoba, Spain
Sangre (Barc); 26(5B):700-717 1981
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Kirurgisk-gastroenterologisk afdeling, Bispebjerg hospital, Copenhagen, Denmark
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Huang PC, Sheridan RB
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12. THE HEALTH EFFECTS AND ECOLOGICAL SIGNIFICANCE OF CHLORINE RESIDUALS IN WATER.
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Univ. Tennessee, Univ. Station 8163, Knoxville, TN, 37916
Chemosphere; 10(10):1163-1175 1981

13. CHEMICAL AND ENVIRONMENTAL AGENTS IN GASTROINTESTINAL CARCINOGENESIS.
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Lab. Digestive Tract Carcinogenesis, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Clin Gastroenterol; 10(3):755-771 1981

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Dept. Pathology, Lab. Experimental Oncology, Stanford Univ., Stanford, CA, 94305
J Supramol Struct Cell Biochem; 16(1):91-103 1981

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15. ROLE OF HORMONES INCLUDING DIETHYLSTILBESTROL (DES) IN THE PATHOGENESIS OF CERVICAL AND VAGINAL INTRAEPITHELIAL NEOPLASIA.
Robboy SJ, Truslow GY, Anton J, Richart RM
Dept. Pathology, Massachusetts General Hosp., Boston, MA, 02114
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Dept. Microbiology, Pennsylvania State Univ. Coll. Medicine, Hershey, PA, 17033
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Nasemann T
Univ.-Hautklinik Eppendorf, Martinistr. 52, D-2000 Hamburg 20, W. Germany
Hautarzt; 32(11):601-606 1981
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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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HE 20.3173/2:

PREVALENCE OF GI CANCER IN HUMAN POPULATIONS

1. INCIDENCE OF MALIGNANT NEOPLASMS OF DIGESTIVE ORGANS.

Zemla B, Kolosza Z, Czech J, Jamrozik W
Instytut Onkologii, ul. Wybrzeze Armii Czerwonej 15, 44-101 Gliwice, Poland

Wiad Lek; 34(13):1077-1083 1981

Epidemiological data on the incidence of malignant neoplasms of the digestive organs in the population of Zabrze and its suburbs between 1965-1975 are presented. Malignant neoplasms of digestive organs were diagnosed in 199 men and 205 women. Esophageal tumors were diagnosed in 6 men and 4 women, gastric tumors in 130 men and 71 women, colon tumors in 14 men and 41 women, rectal tumors in 11 men and 23 women, hepatic tumors in 11 men and 20 women, gallbladder tumors in 5 men and 23 women, and tumors of the pancreas, peritoneum and undetermined localizations in 20 men and 27 women. The standardized incidences per 100,000 population were 1.64 for esophageal tumors, 32.96 for gastric tumors, 3.45 for colon tumors, 2.86 for rectal tumors, 2.81 for hepatic tumors and 50.96 for all localizations in men. The corresponding incidences in women were 0.30, 11.10, 6.54, 3.60, 3.07 and 32.03. The incidence of malignant tumors of the digestive organs, especially of the stomach, was significantly lower in the autochthonous populations of districts supplied with water of relatively high hardness, ie, with high levels of magnesium salts, chlorides and sulfates, than in the immigrant population. (8 Refs) (In POL)

2. INCREASING FREQUENCY OF ESOPHAGEAL CANCER AMONG BLACK MALE VETERANS.

Rogers EL, Goldkind L, Goldkind SF
Veterans Admin. Medical Center, 3900 Loch Raven Blvd., Baltimore, MD, 21218

Cancer; 49(3):610-617 1982

Between the years of 1975 and 1979, the frequency of diagnosis of esophageal cancer has doubled at the Baltimore VA Medical Center due to a rapid increase of esophageal cancer among black males. This increase was not related to increased yearly hospital admission rates, percentage of black patients admitted yearly, or increased use of the hospital for chronic disease processes. Detailed chart review and comparison with consecutive medical admissions as controls revealed heavy alcohol use and urbanization to be risk factors experienced more frequently by black than white male veterans. A serious question needs to be quickly answered: Does the rise of esophageal cancer at the Baltimore VAMC reflect a rise among black males only in Baltimore or does it reflect a rise nationwide among black males with a history of previous employment in the armed forces? (Author abstract) (19 Refs)

3. CANCER EPIDEMIOLOGY.

Sancho-Garnier H, Flamant R
Departement de Statistique Medicale et Unite de Recherches Statistiques, 94800 Villejuif, France

Rev Infirm; 31(17):19-27 1981

Standardized cancer mortality rates for 1973 yr set France in third place, behind West Germany, England, and Wales. In France, the overall cancer mortality was 221 per 100,000 inhabitants but men were affected twice as often as women. The increase of cancer mortality rate from 1954-1976 was attributed to the increase in cancer deaths among men due to lung cancer and cancers of the upper gastrointestinal and respiratory tracts. Deaths from cancer represented about 20% of general mortality and a third of the deaths for men in the 55-75 yr range and for women in the 35-55 yr range. Analytical epidemiology has determined the probable causative factors of various types of cancers. These etiological agents include tobacco, pollution, ultraviolet or ionizing radiation, alcohol, nutrition, hormones, infections, and immunological and genetic factors. Cancer has also been linked to certain immunosuppressive and cytotoxic drugs. Resistance to epidemiological data is steadfast not only because pleasurable pursuits such as drinking and smoking are involved but also because the economic consequences of change are staggering. However, more than half of the cancer cases would be affected by alcohol and tobacco campaigns and by the early screening and treatment of cancers of the breast and uterus. (17 Refs) (In FRE)

4. EPIDEMIOLOGICAL AND IMMUNOLOGICAL ASPECTS OF GASTROINTESTINAL CANCER IN ISRAEL (MEETING ABSTRACT).

Shani A, Bentwich Z
Unit of Oncology, Department of Medicine, Kaplan Hospital, Rehovot, Israel

UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Gastrointestinal (GI) cancer in Israel is significantly less common among Jews of Oriental (O) origin compared to Jews of European (E) origin. The purpose of our study was to determine whether such differences were in any way related to the immune functions. In a propective study of 188 newly diagnosed GI cancer patients several immune parameters were determined and correlated with disease stage and course and with the ethnic background. Patients were studied preoperatively and every 4 mo subsequently. Age, sex and ethnic backgroud matched controls were studied in parallel. The main positive findings were: a) Increased spontaneous (background) thymidine uptake of peripheral blood lymphocytes of (0) vs (E) patients accounting also for differences observed in the response to mitogens between the two ethnic groups; b) Higher grade of malignancy as assessed by nuclear grading in (0) vs (E) patients; c) A trend for more immune reactivity at tumor site among (0) vs (E) patients. In addition, a) The diagnostic efficacy of the leucocyte adherence inhibition assay (LAI) in the preoperative diagnosis of colorectal carcinoma was 31/54 (57%) and this rate increased to 70% when it was combined with determination of carcinoembryonic antigen. b) Antinuclear antibodies (ANA) were more common among patients and correlated with tumor dissemination. c) No significant differences were found between the various groups in the circulating immune complexes and blood lymphoid populations. It would thus seem that stronger immune reactivity towards the tumor is present in the Oriental host and would possibly explain why this ethnic group is better protected from GI cancer. (no Refs)

5. DESCRIPTIVE EPIDEMIOLOGY OF GASTRIC CANCER IN THE DISTRICT OF BASSANO, 1957-1976 (MEETING ABSTRACT).

Mastrangelo G, Zambon P, Nitti D, Scarparo F, Acqua A, Rossi R
Universita di Padova, Padova, Italy
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

The purpose of the present study is to describe the geographical distribution of Gastric Cancer (GC) by age and sex in the Unita Sanitaria Locale (health authority area) of Bassano, situated in the north-eastern part of Italy (population 115,380 in 1971). At present the economic characteristic is widespread small industry, whereas in the past the area covered was mainly rural. The age-standardized mortality rates of GC during the period 1957-1966 were 20.98/10(5) for yr for males and 11.95/10(5) for yr for females; during the successive period 1967-76 such rates were 12.16/10(5) for males and 7.14/10(5) for females. The age-specific mortality rates, strongly increasing with age, showed a pattern frequently observed when an exogenous agent, acting continuously throughout life, is believed to be the major etiological stimulus. The geographic distribution of observed and expected cases of GC in the 20 towns of district fails to indicate a definite relationship with the characteristic of economic development, eg percent of employed in industry or agriculture, in each town. (no Refs)

6. INCIDENCE OF CANCER OF THE RECTUM IN THE PROVINCE OF PADOVA (MEETING ABSTRACT).

Lise M, Cagol PP, Andriulo B, Buzzatti A, Da Pian PP, De Marchi F, Mastrangelo G
Istituto Patologia Chirurgica III, Universita di Padova, Padova, Italy
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Data concerning rectal cancer morbidity for 7 yr (1974-80) were obtained from registries of Pathology Laboratories of the province of Padova. For each patient the following data were collected: 1) histological diagnosis; 2) sex; 3) date of birth; 4) date of diagnosis; 5) residence; 6) department of admission. Cases diagnosed before 1974, cases with uncertain diagnosis, and patients living in another province were excluded. Eight administrative areas of the province were used as geographical subdivision. The number of the cases observed in each area was compared with the expected number. The ratio between observed and expected cases is indicated as standarized incidence ratio (SIR), and its deviation from 1.00 was tested by the chi-square test. Annual incidence rates for each sex were calculated for the entire province, the city of Padova and the rest of the province. Rates were standardized with the direct method on the basis of Segi's world population. Confidence limits of 95% were calculated on the assumption of Poisson distribution. Both in the city and province and increasing trend with age was observed, with a peak in older ages. Males presented a higher risk to develop cancer of the rectum in all the province. The observed: expected ratio of cancer of the rectum resulted significantly lower in the northern areas and significantly higher in the Padova's urban area. A well defined area of particularly low incidence of rectal cancer was identified. Therefore it seems justified to perform an environmental research of etiological factors. (no Refs)

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN GI CARCINOGENESIS

7. MALIGNANT TUMORS AFTER CHRONIC EXPOSURE TO VINYL CHLORIDE.

Emmerich KH, Norpoth K
Inst. Pathology, Univ. Munster, Domagkstr. 17, D-4400 Munster, W. Germany
J Cancer Res Clin Oncol; 102(1):1-11 1981

Correlations between exposure to vinyl chloride and the development of malignant tumors in the liver have been known since 1974 and have been confirmed by many an experimental investigation. Based on the evaluation of mortality statistics from nine different countries an increased incidence of malignant tumors of the lung, the gastrointestinal tract, and the central nervous system (CNS), and of malignant lymphomas is documented in connection with exposure to vinyl chloride. Statistically significant increases, however, are only found in the incidence of malignant liver tumors. Metabolism and toxicology of vinyl chloride are discussed in detail. (Author abstract) (78 Refs)

8. A STUDY OF THE MORTALITY OF CORNISH TIN MINERS.

Fox AJ, Goldblatt P, Kinlen LJ
Medical Statistics Div., Office of Population Censuses and Surveys, London, England
Br J Ind Med; 38(4):378-380 1981

Increased mortality from cancer of the lung has been found in several studies of miners exposed to high levels of radioactivity in underground air. In view of their exposure to raised levels of radiation, we have studied the mortality of a group of men recorded as Cornish tin miners in 1939. Using occupational description, a crude classification of exposure was derived for these miners. The meaningfulness of this classification was supported by differences in mortality for silicosis and silicotuberculosis. A twofold excess of cancer of the lung was found from underground miners, while for other categories mortality from this cause was less than expected. This supports the findings of previous studies on exposure to radon and its daughters. An excess of cancer of the stomach was also observed among underground miners. (Author abstract) (15 Refs)

DIETARY AND DIGESTIVE FACTORS IN GI CARCINOGENESIS

9. NUTRITION AND GASTRIC CANCER.

Joossens JV, Geboers J
33, Capucijnenvoer, B-3000 Leuven, Belgium
Nutr Cancer; 2(4):250-261 1981

Statistical methods and data from different countries were used to study the cause of gastric cancer (GC) and stroke mortality. GC has a multifactorial origin. Possible causes include genetic factors, soil, and nutritional and socioeconmic factors. GC mortality rates are decreasing in 23 of 26 countries studied. Results of multiple regression analysis of the GC-stroke mortality relationship are presented. A strong association was observed for each sex separately and for both sexes combined. Lung cancer is also related to stroke mortality. According to a working hypothesis set forth in 1965, salt intake is the predominant linking factor for both GC and stroke mortality. Thus, stroke would be influenced by the relationship between salt and blood pressure; GC would result from the delaying and caustic properties of stomach hypertonicity, possibly producing atrophic gastritis. Atrophic gastritis favors the synthesis of endogenous nitrites and of nitroso-carcinogens. The salt hypothesis offers an explanation for the geographical and time behavior of GC and stroke mortality, and the socioeconomic gradient of both diseases. GC mortality can also be used to provide a rough estimate of the salt intake in a given country and yr. The influence of salt was tested in Belgium through a deliberate attempt to lower the salt intake of the population. The observed decreases in GC and stroke mortality were consistent with the measured decrease in salt excretion. Monitoring 24-hr salt and creatinine excretion in different countries and over a longer period of time is needed. (72 Refs)

10. DIET AND CANCER OF THE LARGE BOWEL.

Zaridze DG
Analytical Epidemiology Programme, Div. Epidemiology and Biostatistics, International Agency for Res. on Cancer, 150 Cours Albert Thomas, 69372 Lyon, Cedex 2, France
Nutr Cancer; 2(4):241-249 1981

Suspected etiological and protective factors in large bowel cancer are reviewed. Incidence of large bowel cancer correlates with consumption of fat, protein or meat. Etiological hypotheses propose that high-fat diet is related to an increased risk of large bowel cancer, while analysis of the geographical distribution of colon cancer in humans. The results of further epidemiological studies do not unequivocally support the hypotheses. Control studies do not confirm an association between diet and the colorectal cancer risk at the individual level. Lack of uniformity among the findings of epidemiological studies concerned with the role of diet could be explained by lack of sensitive and reproducible methods for assessment of diet in epidemiological studies and lack of knowledge of the mode of action of dietary factors responsible either for the development of the tumor or for protection against it. Research on large bowel cancer in humans is focused on the promoting factors. Initiators could be the factors responsible for the individual risk for colon cancer in populations with homogeneous high-fat diet practices. Available data indicate adenomatous polyps and non-invasive carcinoma of the large bowel could remain stationary. Fu ture epidemiological research on diet and large bowel cancer should deal with more precisely defined hypotheses in which the multifactorial nature of the tumor would be taken into account. (49 Refs)

11. RELATION BETWEEN CANCER DEATH AND FOODS CONSUMPTION --- SEVEN SITES IN DIGESTIVE ORGANS (MEETING ABSTRACT).

Nagai M, Hara N, Sakata K, Hashimoto T, Yanagawa H
Department of Public Health, Jichi Medical School, Tochigi, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

The areal difference of the mortality from cancer of 7 sites of digestive organs and consumption of foods in 46 prefectures and their capital cities were observed and analyzed by correlation and factor analysis. The standardized mortality ratios (SMR) for male were calculated over 10 yr (1969-'78). The variables on food consumption were selected from two surveys conducted by Prime Minister's Office. The foods statistically suspected as risk factors are: 1) pork, oil and shochu for esophagus cancer; 2) fresh fishes, salted fishes, vegetables and alcoholic drinks for stomach cancer; 3) alcoholic drinks, salted fishes, vegetables, bread, milk, butter, margarine, ketchup, beer and fresh fishes for colon cancer; 4) fresh fishes, salted fishes, salt and sake (2nd class) for rectal cancer; 5) pork, sake (2nd) and green tea for bile ducts cancer; 6) salted fishes, vegetables, alcoholic drinks, oil and fresh fishes for pancreas cancer; 7) beef, chicken, egg and vinegar for liver cancer. (no Refs)

12. DIET AND CANCER OF THE ESOPHAGUS.

Mettlin C, Graham S, Priore R, Marshall J, Swanson M
Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY
Nutr Cancer; 2(3):143-147 1981

The reported dietary, alcohol consumption, and smoking habits of 147 white male patients diagnosed with cancer of the esophagus were compared with the reports of 264 white male patients of comparable ages with diagnoses other than cancer. The associations of cigarette and alcohol use as risk factors were examined. Beer drinking was the beverage most associated with risk elevation. Persons reporting their occupation as laborers, service personnel, and operatives were considered as having significantly elevated relative risk (RR). RR associated with levels of vitamin A intake ranged from 0.68-1.28. Vitamine C intake was more highly associated with disease status. Because both vitamin A and vitamin C intake are highly dependent on the fruit and vegetable consumption habits of patients, the association of the simple reported frequency of consumption of fruit and vegetables was examined. RR ranging from 0.52-2.47 indicate a 4.75-fold increase in RR when consumption of fruits and vegetables was less than 40x/mo and was compared to a reported intake of greater than 81x/mo. The increase in risk represents a gradient consistent with a hypothetical dose-response relationship. No significant modification of the effect was observed across smoking, drinking, or smoking and drinking specific categories. No significant modification of the effect was observed in analyses of high risk groups of laborers, service and operative workers and other occupations, suggesting that the effects of diet may be independent of social class as measured by type of occupation. The findings of this investigation are consistent with evidence of lower risk associated with vegetable consumption in instances of colon, lung, bladder, oral, and laryngeal cancers, and with evidence for animals of tumor inhibition by vegetable properties. (18 Refs)

13. CARCINOGENESIS OCCURRING NATURALLY IN FOOD.

Hilker DM
Dept. Food Sciences and Human Nutrition, Univ. Hawaii, Henke Hall 224, 1800 East-West Road, Honolulu, HI, 96822
Nutr Cancer; 2(4):217-223 1981

The role of carcinogens which are metabolites of microorganisms infecting plants during harvesting and storage, products of the normal metabolism of plants, products of chemical changes occurring during processing, preservation, or preparation, and which are picked up from the environment through contaminated water or soil is discussed. Some of the most potent carcinogens are fungal metabolites such as aflatoxin B1, 4-ipomeanol, luteoskyrin, methylhydrazine, and ethylcarbamate. The pyrrolizidine alkaloids safrol, oil of calamus, cycasin, thiourea, and tannin also have carcinogenic activity. Polycyclic hydrocarbons, particularly benzo(a)pyrene (BP), are commonly found in food. BP can be found in plant food, seafood, and in meats. Polycyclic hydrocarbons including BP are formed by smoking meat and fish. Epidemiological studies indicate the high incidence of gastric cancer in the areas of the world where smoked fish are common in diets. Vitamin A and certain of its analogues can prevent the carcinogenic activity of BP and some other polycyclic aromatic hydrocarbons. The role of vitamin A appears more important when one considers that the diets of people in areas with high incidence of gastric cancer are low in vitamin A. The interrelated effects of vitamin A-poor diets, consumption of carcinogenic hydrocarbons, and the incidence of cancer need further study. Information is also needed on the amount of carcinogenic chemicals an individual must consume in order to exhibit cancer and on the interrelated effects of other dietary constituents. (59 Refs)

14. AN EPIDEMIOLOGICAL STUDY ON THE POSSIBLE ASSOCIATION BETWEEN INTAKE OF BROILED FISH AND CANCER (MEETING ABSTRACT).

Ikeda M, Yoshimoto K, Yoshimura T, Kono S, Kato H, Kuratsune M
Department of Public Health, Fac. of Medicine, Fukuoka, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

Yr ago, the Radiation Effects Research Foundation investigated 7,553 subjects for dietary habits such as frequency of consumption of broiled fish, milk, and others. Therefore, the possible association between these habits and their cancer deaths seen during 11 yr was investigated by the linear multiple stepwise regression analysis. Frequent consumption of broiled fish was significantly positively associated with deaths from all sites of cancer and those from gastric cancer. Liver cancer was also associated with this habit but with no statistical significance. (no Refs)

15. DIETARY FIBER: IS IT REALLY HELPFUL?

Burkitt DP
Unit Geographical Pathology, St. Thomas's Hosp., London SE1, England
Geriatrics; 37(1):119-122,126 1982

Fiber in the diet is discussed; topics include defects of Western diet, cancer, diabetes, gallstones, obesity, ischemic heart disease, and history of disease. Culturally determined dietary patterns appear to be responsible for the high prevalence in Western societies of major diseases such as colon cancer, atherosclerotic heart disease, and diabetes. Five fundamental dietary changes that distinguish modern Western diets from those of the Third World. are reduction in consumption of carbohydrate, particularly starch, increased consumption of sugar, increased consumption of fat, increased consumption of salt, and reduced consumption of fiber and replacement of fiber derived from cereals, legumes, and tubers with that from fruits and leafy vegetables. Cereal fiber has a much greater influence on bowel content and behavior than that from fruits and leafy vegetables. Fiber has important mechanical and metabolic functions in addition to influencing the bacterial flora in the large bowel. Fiber-rich diets are believed to protect against large-bowel cancer and may provide some general protection against all diet-related cancers. The role of dietary fiber in other diseases is reviewed. Diets should include more starch, less sugar, less fat, more fiber, and less salt. (10 Refs)

16. CARCINOGENICITY OF CARRAGEENAN.

Hopkins J
British Industrial Biological Res. Assoc.
Food Cosmet Toxicol; 19(6):779-781 1981

The carcinogenic potential of the food stabilizer carrageenan is discussed. Carrageenan has been identified as a cocarcinogen in studies with rats, enhancing methylnitrosourea-, azoxymethane- and dimethylhydrazine-induced colonic carcinoma. Carrageenan may also produce colonic carcinoma when used alone. (no Refs)

17. NUTRITION AND CANCER. INTRODUCTORY REMARKS.

Carroll KK
Univ. Western Ontario, Ontario, Canada
Nutr Cancer; 2(4):197-198 1981

Food consumption data, methods of food analysis, animal models, recommendations regarding cancer at specific sites (colon, breast, stomach, other sites), and data on cancer incidence and mortality have been reviewed. No dietary recommendations to the public have been made. Further experiments are needed to clarify the role of diet in carcinogenesis. (no Refs)

18. CHOLECYSTECTOMY AND CARCINOMA OF THE COLON.

Linos DA, Beard MC, O'Fallon W, Dockerty WB, Beart RW, Kurland LT
Mayo Clinic, Rochester, MN
Curr Surg; 38(6):391-393 1981

To determine whether secondary bile acids play a role in the etiology of cancer of the colon, 1,681 patients (460 men, 1,221 women) who underwent cholecystectomy for cholelithiasis were followed up for 1-29 yr. Carcinoma of the colon and rectum was detected in 42 patients (13 men, 29 women). The risk of right colon cancer in women subjected to cholecystectomy was 2.1x greater that the risk for the control female population. (8 Refs)

OTHER ETIOLOGIC FACTORS IN GI CARCINOGENESIS

19. HYPERPLASTIC POLYPS OF THE STOMACH AND GASTRIC CANCER (MEETING ABSTRACT).

Dalaiti A, Calzoni P, Minarini A, Gizzi G, Grigioni W, Di Febo G, Biasco G
Cattedra di Clinica Medica III, Universita di Bologna, Bologna, Italy
Medicina Domani Genova '81: Ulcera Peptica e Cancro Gastrico, April 23-24, 1981, Genoa, Italy. University of Genoa 126 pp., 1981.

Since certain observations suggest that hyperplastic polyps of the stomach, while not being structures with preneoplastic characteristics, can be considered as indicators of high risk for cancers of the stomach, we have conducted a retrospective analysis based on a review of: a) 81 cases (49 females, 32 males, ages 20-87) of hyperplastic polyps of the stomach diagnosed after polypectomy or endoscopic macrobiopsy, b) 43 cases (25 females, 32 male, ages 33-81) of initial stage stomach cancer. This portion of the study was performed by reviewing the biopsies of the gastric surgical specimen. In 6 subjects with hyperplastic polyps there was a coexisting carcinoma at another site in the stomach (7.4%) and in 17 cases of stomach cancer 1 or more hyperplastic polyps were present at a distance from the tumor site (39.5%). The results support the hypothesis that hyperplastic polyps can serve as markers of a high risk of gastric cancer. However, on the basis of these findings alone the possibility that the formation of hyperplastic polyps could also be the result of nonspecific phenomena secondary to the development of a carcinoma cannot be excluded. We believe the only way to resolve the matter is by endoscopic and histobioptic follow-up of patients with hyperplastic polyps of the stomach. (1 Ref) (In ITA)

20. MULTIPLE MALIGNANCY WITH A FAMILIAL TENDENCY.

Forrest J, Slaney G, Crocker J, Hallam J, Taylor AM
Dept. Surgery, Univ. Birmingham, Birmingham, England
Clin Oncol; 7(4):357-364 1981

The patient described died in 1980 from a carcinoma of the lung which was his ninth primary malignancy. Previous cancers had arisen in the skin, cecum, ileum, kidney, bladder, rectosigmoid colon, descending colon and stomach. All these tumors with the exception of the bladder were treated by surgical resections over a 16 yr period and at autopsy no evidence of recurrence of any of them was evident. One other 'tumor' also reported as a carcinoma and arising in the patient's larynx proved on review to have controversial histological features and is therefore not included. The male line of this man's family had a very high cancer record, and three members of two generations have died in their fourth and fifth decades with bowel cancer. Other benign lesions treated surgically included Crohn's ileitis and prostatic hyperplasia. Cellular studies failed to reveal anything exceptional in the response of his cultured cells to three different types of DNA damaging agent (x-rays, UV light or mitomycin C). (Author abstract) (3 Refs)

21. FREQUENCY AND EVOLUTION OF PRECANCEROUS AND DYSPLASTIC LESIONS IN THE STOMACH.

Martin ED
Dept. Pathology, Universite Paris, Hopital A. Beclere, Sud. 92141 Clamart, France
Excerpta Med Int Congr Ser; 555:225-230 1981

Precancerous conditions and lesions of the stomach are discussed with respect to hyperplastic and proliferative lesions and inflammatory and atrophic chronic gastritis. Gastric polyps are rare and are generally divided into two groups: the well differentiated or hyperplastic polyps rarely evolving into carcinoma, and the adenomatous or villous polyps capable of evolving into carcinoma in 15-40% of cases. The av frequency of the association of diffuse or localized hypertrophic gastritis of Menetrier to gastric carcinoma (GC) is about 5-6%. Of the 37 cases of gastritis glandularis and cystica profonda, 14 presented with foci of GC. The development of GC from gastric ulcers or scars of ulcers is rare (less than 1.96%). In 3.4-11% of gastrectomy patients, GC appears from 12-25 yr after gastrectomy. The risk of GC in patients with pernicious anemia is 5-20x that of the general population. The aforementioned lesions become precancerous when they are associated with intestinal metaplasias and dysplasias. It was estimated that 80% of the GC are found in patients without any known precancerous conditions. Whether all GC are preceded by precancerous lesions is unknown. The possibility that chronic gastritis is precancerous is discussed. The time between the discovery of chronic gastritis and the development of GC appears to be long, often more than 10 yr. More large and precise epidemiological, endoscopical, and histological coordinated studies are warranted. (19 Refs)

22. NITRITE AND NITROSAMINES IN GASTRIC JUICE: RISK FACTORS FOR GASTRIC CANCER?

Schlag P, Bockler R, Peter M
Dept. Surgery, Univ. Ulm, Steinhovelstr. 9, D-7900 Ulm, W. Germany
Scand J Gastroenterol; 17(1):145-150 1982

Nitrite and nitrosamine concentrations have been measured in 108 patients undergoing gastroscopy as a part of routine gastrointestinal investigations. The nitrite and nitrosamine values of 20 patients with duodenal and 11 patients with benign gastric ulcer were within the range of the values of 26 normal subjects. The nitrite and nitrosamine concentrations in 32 patients with inflammatory changes of the gastric mucosa were slightly higher than normal values and correlated with the progressive degrees of the severity. In 19 patients with atrophic gastritis the concentrations of nitrite and nitrosamines were significantly elevated in comparison with those of all other groups. Our data suggest a relationship between the constant exposure of an already damaged gastric mucosa to N-nitroso compounds and the known high incidence of gastric cancer in atrophic gastritis. (Author abstract) (11 Refs)

23. SMOKING AND ALCOHOL INTAKE IN ESOPHAGEAL CANCER - A COMPARISON OF ESOPHAGEAL AND GASTRIC CANCER.

Nishikage S, Hara M, Tsurumaru A, Akiyama H
Dept. Pathology, Toranomon Hosp., Japan
Gan No Rinsho; 27(15):1788-1795,A-87 1981

Of 168 patients with cancer of the esophagus, 14 (8.3%) had multiple cancers; of 818 with stomach cancer, 45 (5.5%) had multiple cancers. Most patients with esophageal cancer had habits of excessive smoking and alcohol intake. Excessive smoking and alcohol intake were rare in gastric cancer patients. (43 Refs) (In JPN)

24. IDENTIFICATION OF RISK FACTORS IN NEOPLASTIC PATHOLOGY OF THE STOMACH (MEETING ABSTRACT).

Alvisi V, Pavani F, Ruina M, Loponte A, Tralli M, Pollinzi V
Istituto di Clinica Medica Generale E Terapia Medica, Universita di Ferrara, Ferrara, Italy
Medicina Domani Genova '81: Ulcera Peptica e Cancro Gastrico, April 23-24, 1981, Genoa, Italy. University of Genoa 126 pp., 1981.

Increasing recognition, thanks to the routine utilization of endoscopy, of precancerous stomach lesions poses the problem of which patients to regard as high risk and when they should be subjected to preventive surgical treatment. The authors' experience is based on a case series of 56 patients with precancerous diseases or non-infiltrating cancers; 34 were male and 22 female, their ages ranged from 35 to 66 with an av of 52 yr. A broader study of the chief factors which might be associated was conducted involving such risk factors for stomach neoplasms as familial neoplasms, polygenic genetic factors (blood groups), survey of complicating diseases, gastric juice hydrochloric acid secretion characteristics, features of hormonal feedback, topographic features of the lesions, macro- and microscopic appearances of the gastric mucosa, immunologic aspects (humoral and histologic), dietary habits, social class, work environment . From the observations made it turned out that among the features listed above those which recurred most often were: hydrochloric acid hyposecretion, 82.1% of the cases; chronic atrophic gastritis, 64.3%; blood group A, 67.8% of the cases. These data would therefore seem highly significant for defining the group of patients who are theoretically most exposed to the risk of developing a gastric neoplasm. (no Refs) (In ITA)

25. GASTRIC CANCER AFTER VAGOTOMY AND EXCISION FOR GASTRIC ULCER.

Haukland H, Johnson JA
Dept. Surgery, Inst. Clinical Medicine, Univ. Tromso, Tromso, Norway
Eur Surg Res; 13(5):371-375 1981

A follow-up examination of 152 patients with gastric ulcer treated with vagotomy, ulcerectomy and drainage showed that 4 of the patients manifested gastric cancer 5-7 years after the operation. A simultaneous follow-up of a parallel series of 269 patients with duodenal or pyloric ulcer treated with vagotomy and drainage in the same surgical unit did not reveal a single case of gastric cancer development. The observations seem to indicate that there is a greater risk of cancer development in the ulcerectomized and vagotomized stomach. (Author abstract) (13 Refs)

26. PREDISPOSITION OF THE RESECTED STOMACH FOR MALIGNANCY.

Rakovec S, Kovic M
Medical Center, Univ. Surgical Hosp., Ljubljana, Yugoslavia
World J Surg; 5(5):725-727 1981

The cases of 62 patients treated for carcinoma of the gastric stump following resection for benign causes are described. The group represented 4.6% of all stomach cancer patients treated and 2.6% of all those who underwent partial resection for peptic disease. Females were only 3/62 of the patients. The av history of complaints lasted 3.5 mo; most frequent presenting symptoms were anemia, weight loss, dysphagia, epigastral pain, aversion to food, and weakness. Carcinomas were located in the anastomosis (60%), at the cardia of the stomach (36%), or elsewhere on the gastric stump. Adenocarcinoma was the most frequent type of carcinoma (61%). Survival rate after resection averaged 14 mo. The high percentage of inoperable patients indicates that diagnosis was too late. Avoidance of gastric resection in duodenal ulcer cases, and radiological and gastroscopical examination of the residual stomach, are recommended. (13 Refs)

27. MALIGNANT GASTRIC ULCER.

Neaman A, Laser A, Dalperi G, Avidor A, Kadish A
Inst. Gastroroentgenology, Bellinson Medical Center, Tel Aviv, Israel
Harefuah; 101(3):53-54 1981

Seventy-five patients with gastric ulcer were examined with fiberoptic endoscopy. Patients with ulcers involving malignant infiltrative tumors of the stomach were not included in the study. The ulcers were examined macroscopically, 8-10 biopsies from the margins and floor of each ulcer were taken, and the tissue was examined histologically. In 10 of the 75 patients (13.4%), biopsy specimens met pathological criteria for malignant ulcer. Eight of these were adenocarcinoma, two of them lymphoma. Macroscopically, eight of the ten malignant ulcers were thought to be malignant based on the following criteria: diameter greater than 2 cm, rough margins, irregularities of the ulcer floor. Two of the ten malignant ulcers appeared benign macroscopically. Many of the patients examined had upper gastrointestinal tests prior to endoscopy; radiologically many of the malignant ulcers were not identified. Symptom profiles of those patients with benign ulcers and those with malignancies were indistinguishable. The percentage of patients with malignant ulcers (13.4%) is significantly higher than the percentage reported elsewhere (5%), perhaps because the reported figure is derived from studies not based on endoscopic diagnosis. Endoscopy and multiple biopsies for all patients with gastric ulcer are suggested. (17 Refs) (In HEB)

28. HEREDITARY COLON CANCER. IDENTIFYING THE HIGH-RISK PERSON.

Lynch HT, Lynch PM, Albano WA, Lynch JF
Dept. Preventive Medicine, Creighton Univ. Sch. Medicine, 2500 California St., Omaha, NE, 68178
Consultant; 22(1):331,333-334,336-337,339,342-343 1982

Identification and management of hereditary colorectal cancer are described, with emphasis on surveillance and follow-up protocols developed for family members at high risk for the malignancy. Two major subtypes of hereditary colorectal cancer exist: those with and those without multiple adenomatous colonic polyps. Polyposis coli syndromes account for less than 1% of all colorectal cancers and include a spectrum of syndromes with and without extracolonic signs. Cutaneous and osseous tumors may be present in Gardner's syndrome; nervous system tumors may appear in Turcot syndrome. Identification of a patient affected with familial polyposis coli is important; the disease is associated with an easily identifiable biological marker, polyps, that precedes malignant change. An expected one of the patient's parents, one-half of his siblings, and one-half of his children may be similarly affected. The polyposis phenotype is usually first expressed in the rectosigmoid area by the second decade, years before cancer occurs. Family surveillance, a protocol for diagnosis and management of hereditary colon cancer, and the physician's responsibility are discussed. (5 Refs)

29. JUVENILE POLYPOSIS: BENIGN DISEASE OR POTENTIALLY MALIGNANT?.

Potet F, Barge J
Service d'Anatomie et Cytologie Pathologiques, Hopital Beaujon, F-92118 Clichy Cedex, France
Gastroenterol Clin Biol; 5(12):1133-1135 1981

The association of juvenile polyps (JP), familial polyposis, rectal and colonic carcinomas is discussed. Colectomy has rarely been used to treat JP due to lack of evidence suggesting their malignant potential. Studies are described in which JP were associated with familial polyposis and/or a family history of colonic neoplasms, with adenomatous polyps, and with colonic carcinoma. The potential of JP for neoplastic transformation is discussed. (22 Refs) (In FRE)

30. GASTRITIS, PEPTIC ULCER DISEASE, INFLAMMATORY BOWEL DISEASE, AND STOMACH AND COLON CANCERS - ARE THEY ALL CAUSED BY VIRAL INFECTIONS?

Waldum HL, Bjorvatn B, Burhol PG
Dept. Medicine, Univ. Hosp. Tromso, Tromso 9012, Norway
Med Hypotheses; 7(11):1329-1338 1981

A hypothesis considering that chronic gastritis and ulcerative colitis are induced by viral infections, and that such chronic infection of the mucosa may lead to ulceration and occasionally cancer, is proposed. Since gastric ulcers occur almost exclusively together with gastritis, it is conceivable that both disease may reflect an infection with the same virus, perhaps cytomegalovirus; also is considered that the increased vagal tone in patients with duodenal ulcers may be caused by viral involvement of the vagal ganglion. In patients with dy-

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spepsia without gastritis or peptic ulcer, the virus may remain in the vagus ganglion, affecting afferent nerves leading to pain and discomfort. Gastric cancer occurs almost exclusively in patients with gastritis, and patients with gastric ulcer disease have an increased risk of developing gastric cancer. In addition, patients with immune defects have an increased frequency of gastritis and gastric cancer. A common etiology of gastritis, gastric ulcer, and gastric cancer is suggested. Duodenal ulcers and Crohn's disease may be due to activation of latent viral infection of the corresponding neural ganglions, with subsequent migration of virus along the nerves to the gut wall. Ulcerative colitis may be caused by cytomegalovirus. If ulcerative colitis has a viral etiology, it is reasonable to assume that the same virus may predispose to malignant cell transformation in the colon mucosa. Colon polyps may also be caused by chronic viral infections. The similarities between gastritis, gastric ulcer disease, gastric cancer, duodenal ulcer disease and non-ulcer dyspepsia on one hand and ulcerative colitis, colon cancer, Crohn's disease and irritable colon on the other, are discussed. (46 Refs)

INDUCTION OF GI CARCINOGENESIS IN ANIMALS

31. PRODUCTION OF TUMORS IN THE UPPER G.I. TRACT OF BEAGLES BY ENNG (MEETING ABSTRACT).

Ichiki H, Tasaka K, Orima H, Kurihara M, Miyasaka K, Izumi T, Sasaki Y, Kamano T, Yasui A
Nippon Veterinary and Zootechnical College, Nippon, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

Twenty home bred beagles received N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG) with Tween 60 soln mixed with pellets for a yr (Kurihara's method). At 14 mo, melanoma on the lip of dog No 9 was resected and dog No 14 suffered from a mandibular tumor. At 15 mo, dog No 4 was sacrificed because of emaciation by laryngeal carcinoma (ca). At 20 mo, multiple polypoid tumors or ulcerative lesions of stomach were found in 17 dogs and gastric carcinoma confirmed in 12 dogs by autopsy or biopsy. Moreover, esophageal tumors were recognized in 13 dogs and 9 of them have suffered from Borr, II type ca. In this series, malignant lesions were more prominent in the mouth and esophagus than stomach, compared with previous reports by Kurihara. (no Refs)

32. EARLY CHANGES OF DOG ESOPHAGEAL MUCOSA INDUCED BY N-ETHYL-N'-NITRO-N-NITROSOGUANIDINE.

Takubo K, Shisa H, Futatsuki K, Sasajima K
Dept. Pathology, Saitama Cancer Center Res. Inst., Ina-machi, Kitaadachi-gun, Saitama-ken 362, Japan
Gan; 72(6):880-885 1981

Early changes in the esophageal mucosa of dogs induced by N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG) were studied. Seven 1-yr-old beagle dogs were given a solution of 250 ug ENNG/ml to drink ad libitum for 4 mo. Three different kinds of lesions (10 erosive carcinomas, 4 slightly elevated microcarcinomas and 19 leukoplakias) were recognized. These three kinds of lesions were not located adjacent to one another, and were surrounded by almost normal stratified squamous epithelium. The foci of the carcinomas revealed an abrupt transition to normal epithelium and were considered to have arisen abruptly from normal esophageal epithelium. The histogenesis of squamous cell carcinomas of the esophagus in dogs may differ from that in man. (Author abstract) (17 Refs)

33. PROMOTING EFFECTS OF HYDROGEN PEROXIDE UPON DUODENUM CARCINOGENESIS IN RATS (MEETING ABSTRACT).

Hirota N, Yokoyama T
Department of Pathology, Jichi Medical School, Tochigi, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

In an attempt to investigate the effect of hydrogen peroxide (HP) upon experimental duodenum carcinogenesis, male F344 rats were given ad libitum drinking water containing 1.5% HP for 4 wk prior to methylazoxymethanol acetate (MAM) (25 mg/kg) ip injection, 3 x, once every 2 wk. HP drinking was continuously given during the injection periods except as interrupted by 2-day intervals following each injection in which tap water was given. Then, one group of animals remained on the HP soln over the course of experiment, while HP drinking in another group was discontinued and switched to tap water for the remainder of the experiment. Duodenal carcinoma in the former group was found at 100% at 13 and 17 wk after the last injection, (8/8) and (10/10) respectively in contrast to 25% (2/8) and 30% (3/10) in the latter group given t he same number of wk. In addition, when comparing the total number of carcinomas in each group, carcinogenesis in both duodenum and the upper portion of jejunum in the former group was more pronounced in effect. Treatment with MAM acetate alone induced lower incidence of duodenal carcinoma compared with combination treatment of MAM acetate and HP. Thus, prolonged oral administration of HP following the carcinogen injections to the rats conceivably played a distinct role in promoting duodenal carcinoma formation. (no Refs)

34. SPONTANEOUS REGRESSION OF COLON CANCER IN HIGHLY INBRED WF RATS: GENETIC ANALYSIS.

Saeki K, Miyamoto M, Kitamura H, Hiroyoshi T
Dept. Pathology, Sch. Medicine, Osaka Univ., Osaka, Japan
Gan No Rinsho; 27(13):1623-1626 1981

The occurrence and spontaneous regression of colon cancers in inbred WF rat parents and offspring were studied. When dams of a non-cancer-bearing strain were crossed with males of cancer-bearing, spontaneous regression, or non-cancer-bearing strains, cancers developed in 21%, 14.1%, and 22.7% of the offspring, respectively; spontaneous regression occurred in 35%, 46.8%, and 23.5%, respectively. Results suggest two independent genetic factors, one carcinogenic and one regressive, governing phenotype. (10 Refs) (In JPN)

35. CARCINOGENICITY OF TRICHLOROMETHINE HYDROCHLORIDE (TS-160 SPOFA) AND MORPHOLOGICAL DAMAGE AFTER ITS INTRAAMNIOTIC INJECTION.

Sykora I, Vortel V, Marhan O, Dynterova A
Res. Inst. for Pharmacy and Biochemistry, 533 51 Pardubice, Czechoslovakia
Neoplasma; 28(5):565-574 1981

The cytostatic TS-160 (trichloromethine hydrochloride, tris-/2-chloroethyl/amine hydrochloride) was injected subcutaneously into SPF Wistar rats of both sexes. After all doses used, spindle-cell or even polymorphocellular sarcomas developed at the injection sites in both sexes; after the dose of 0.1

mg/kg daily for 6 months, in 70%; after 0.25 mg/kg, in 79%; and after 1.0 mg/kg weekly for 6 months, in 45% of the rats. Besides, in 21% of the rats receiving the dosage of 0.25 mg/kg mucus-secreting intestinal adenocarcinomas were found. A relationship was apparent between the incidence figures of subcutaneous tumors on the one hand and the daily injection of the low dose versus the intermittent injection of the dose higher by a decimal order on the other hand. In a concurrent test, TS-160 was given to rats in intraamniotic injection on day 18 of pregnancy in doses of 1, 2.5, and 5 ug per embryo. On the first postnatal days, in the affected young rats there were observed morphogenetic disturbances: splanchnocrania and juvenile hair alopecia. These changes became repaired in the further course of postnatal development. (Author abstract) (22 Refs)

36. THE SIGNIFICANCE OF A PHYSICAL FACTOR FOR TUMORIGENESIS IN RAT INTESTINE (MEETING ABSTRACT).

Shindo K, Kotobuki T, Miyamoto T, Kosaki G

2nd Department of Surgery, Osaka University, School of Medicine, Osaka, Japan

Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

The aim of this work is to investigate the influence of stenosis or continuous spasm on intestinal tumorigenesis. One hundred Sprague-Dawley rats were laparotomized and a stenosis was made by a ligature put around the cecum, colon and rectum. Ten mo later the intestine was observed. Eighty-five rats tolerated the experiment and revealed the following histologic lesions: Hyperplastic polyp; Mucosal atypia; Mucosal cyst; Polypoid fold; Lymphoid hyperplasia; and Submucosal lipoma. Various kinds of tumors were made without chemical carcinogen. Intestinal stenosis or spasm promotes tumor formation. (no Refs)

37. METABOLIC FATE OF ASYMMETRIC N,N-DIALKYLNITROSAMINES HAVING A BUTYL GROUP IN THE RAT.

Suzuki E, Okada M

Tokyo Biochemical Res. Inst., Takada 3-14-8, Toshima-ku, Tokyo 171, Japan

Gan; 72(6):910-920 1981

The metabolic fate of N-alkyl-N-butylnitrosamines (alkyl=ethyl, propyl, and pentyl), which induce tumors in the liver and esophagus but do not induce bladder tumors, was investigated in the rat, in order to elucidate any possible correlation between metabolism and the noncarcinogenicity to the urinary bladder of these N-nitrosamines. They were extensively metabolized in the rat, no unchanged compounds being found in the urine. The metabolic pattern of these N-nitrosamines having a butyl chain was essentially similar to that of N,N-dibutylnitrosamine, which induces tumors in the bladder as well as in the liver and esophagus. They were mainly metabolized via omega-oxidation followed by beta-oxidation and/or (omega-1)-oxidation of either of the two alkyl chains. Thus the N-alkyl-N-(3-carboxypropyl)nitrosamine and/or the N-alkyl-N-(2-carboxyethyl)nitrosamine were identified as the principal urinary metabolites. Possible important factors concerned with the induction of bladder tumors by N,N-dialkylnitrosamines are discussed from the metabolic point of view. (Author abstract) (21 Refs)

38. TUMORS OF THE ANAL REGION INDUCED IN MICE PAINTED WITH METHYLAZOXYMETHANOL ACETATE.

Kawaura A, Kumagai H, Shibata M, Izumi K, Otsuka H

Second Dept. Pathology, Sch. Medicine, Tokushima Univ., Kuramoto-cho 3-chome, Tokushima 770, Japan

Gan; 72(6):886-890 1981

The carcinogenicity of methylazoxymethanol acetate (MAM acetate) was examined in 91 BALB/c mice by painting it on the anal region. Carcinomas and adenomas of the perianal sebaceous gland were induced in 23 of 24 male (96%) and 16 of 30 female (53%) mice and keratoacanthoma developed in one of 24 male mice within 30 wk after treatment with MAM acetate. Vascular tumors of the liver and fat tissue of the abdominal cavity also developed in 16 of 24 male (67%) and 3 of 30 female (10%) mice treated with this drug. Microscopic adenocarcinomas were found in the rectal mucosa of 3 of 24 male mice adjacent to the anorectal junction. The sex difference in the incidence of tumors is briefly discussed. (Author abstract) (12 Refs)

MECHANISMS AND MODIFICATIONS OF GI CARCINOGENESIS

39. GLUCOSE INCREASES EXPERIMENTALLY INDUCED COLORECTAL CANCER: A PRELIMINARY REPORT.

Ingram DM, Castleden WM

Univ. Dept. Surgery, Queen Elizabeth II Medical Center, Nedlands, Western Australia, 6009, Australia

Nutr Cancer; 2(3):150-152 1981

The possible role of dietary glucose in the development of 1,2 dimethyl-hydrazine (DMH)-induced experimental colon cancer in rats was studied. The addition of 1.6% glucose to drinking water resulted in significant increase in the number of DMH-induced large bowel tumors in rats, suggesting that a more detailed study should be made on the effect of glucose on the pathogenesis of human colorectal cancer. (11 Refs)

40. EFFECTS OF GLUCOCORTICOID HORMONES ON CELL PROLIFERATION IN DIMETHYLHYDRAZINE-INDUCED TUMOURS IN RAT COLON.

Tutton PJ, Barkla DH

Dept. Anatomy, Monash Univ., Clayton, Victoria, 3168, Australia

Virchows Arch [Cell Pathol]; 38(2):247-251 1981

Adrenocortical hormones have previously been shown to influence cell proliferation in many tissues. In this report, their influence on cell proliferation in the colonic crypt epithelium and in colonic adenocarcinomata is compared. Colonic tumor cell proliferation was found to be retarded following adrenalectomy and this retardation was reversible by administration of hydrocortisone, or by administration of synthetic steroids with predominantly glucocorticoid activity. Tumor cell proliferation in adrenalectomized rats was not promoted by the mineralocorticoid hormone aldosterone. Neither adrenalectomy, nor adrenocortical hormone treatment, significantly influenced colonic crypt cell proliferation. (Author abstract) (21 Refs)

41. ABERRANT AND NONRANDOM METHYLATION OF CHROMOSOMAL DNA-BINDING PROTEINS OF COLONIC EPITHELIAL CELLS BY 1,2-DIMETHYLHYDRAZINE.

Boffa LC, Gruss RJ, Allfrey VG
Rockefeller Univ., New York, NY, 10021
Cancer Res; 42(2):382-388 1982

The alkylating carcinogen 1,2-dimethylhydrazine (DMH) induces colonic tumors with high incidence. The sites of in vivo modification of target macromolecules were studied using [methyl-3H]DMH. Carcinogen binding to subcellular fractions of colonic epithelial cells was analyzed at time intervals ranging from 10 min to 36 hr, with particular emphasis on the alkylation of nuclear constituents. DMH modifies not only nucleic acids but also histones and other DNA-binding proteins in the target cells. Separation of the 3H-methylated amino acids showed aberrant methylation patterns after exposure to [3H]DMH, as compared with methylations observed with [methyl-3H]methionine as a natural methyl group donor. DMH-modified histone H1 contained methylated lysine, arginine, and histidine residues not normally found, and other histones had abnormal methylarginine contents. High-mobility-group proteins and other nuclear proteins contained methyllysine residues not normally detected. Proteins known to be associated with template-active and more accessible DNA sequences, such as the high-mobility group proteins and the multiacetylated forms of histones H3 and H4, were preferentially damaged after exposure to [3H]DMH. The result suggests that carcinogen-induced chromosomal damage is not random and may selectively affect proteins in the actively transcribing or replicating genes in the target cells. That damage affects the amino acids most likely to be involved in DNA binding. (Author abstract) (47 Refs)

42. EXPERIMENTAL COLON CARCINOGENESIS IS FACILITATED BY ENDOGENOUS FACTORS IN THE INTESTINAL CONTENTS.

Lewin MR, Ferulano GP, Cruse JP, Clark CG
Dept. Surgery, Univ. Coll. London, Rayne Inst., University St., London, WC1E 6JJ, England
Carcinogenesis; 2(12):1363-1366 1981

The theory that endogenous factors in the intestinal contents may be pathogenic during large bowel carcinogenesis was tested in the dimethylhydrazine (DMH)-induced rat colon cancer model. Thirty female Wistar rats, each serving as their own control, had a surgical transection of the proximal colon with reanastomosis to the rectum, therby excluding part of the colon from fecal contact. All rats then received a course of DMH (40 mg/kg body wt/wk sc for 10 weeks) while fed on Vivonex. This diet was selected because it lacks known exogenous (dietary) cocarcinogens. It also produces mucosal atrophy in functioning (proximal) colon, to parallel the disuse atrophy induced in the defunctioned (distal) colon. Animals remained on the diet throughout the experiment and were killed when moribund or at 40 weeks. At necropsy, the anatomical distribution, number, size and histological type of colon tumors were compared between functioning and defunctioned colonic segments within the same animal. At autopsy, there were significantly fewer colon tumors in the defunctioned segment (p less than 0.005). Furthermore, there were significantly fewer carcinomas (p less than 0.005) and fewer tumors greater than 1 cm diameter (p less than 0.01) in this segment. The data indicate that endogenous factors in the intestinal contents facilitate chemically-induced colon carcinogenesis. Luminal nutrition may be implicated. (Author abstract) (21 Refs)

43. EFFECT OF DISULFIRAM ON THE TOXICITY AND CARCINOGENICITY OF N-METHYL-N-NITROSOBENZYLAMINE IN RATS.

Schweinsberg F, Burkle V
Hygiene-Institut, Universitat Tubingen, Silchestr. 7, D-7400 Tubingen, W. German y
J Cancer Res Clin Oncol; 102(1):43-47 1981

The concurrent application of disulfiram (710 mg/kg diet; or 200 mg/kg diet) effects a strong enhancement of the toxicity and an acceleration of the formation of esophageal tumors by N-methyl-N-nitrosobenzylamine (10 mg/l drinking water) in female SIV 50 rats. Besides that squamous cell papilloma in the trachea and extended squamous cell metaplasia in the bronchus system with potentially but not safely precancerous nature were seen. (Author abstract) (10 Refs) (In GER)

44. ENHANCING EFFECT OF VAGOTOMY AND PYLOROPLASTY ON GASTRO-INTESTINAL NITROSAMIDE-INDUCED CARCINOGENESIS IN HAMSTERS (MEETING ABSTRACT).

Mori H, Domellof L, Weisburger JH, Williams GM
Department of Pathology, Gifu University, Gifu, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

The possible promoting effect of vagotomy and pyloroplasty on N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) induced carcinogenesis in the gastrointestinal (GI) tract was studied in Syrian golden hamsters on a high fat diet. After truncal vagotomy and pyloroplasty (Group 1) or sham operation (Group 3), 50 ug/ml of MNNG was given for 4 mo in drinking water. Similarly operated (vagotomy + pylorplasty) (Group 2) or non-operated (Group 4) animals without carcinogen administration served as controls. Spindle cell sarcomas of the stomach and small intestine as well as spindle cell proliferation occurred frequently in the MNNG treated hamsters (Groups 1 and 3). A small number of hamsters in Group 1 also developed adenocarcinomas and rosette-forming tumors in GI tracts. Statistically, a significantly higher incidence of tumors of the GI tract or glandular stomach was noted in Group 1 compared to Group. The results suggest that this operation has an enhancing effect on the MNNG carcinogenicity in the hamster. (no Refs)

45. DOES DAILY INTAKE OF SOYBEAN PASTE SOUP REDUCE GASTRIC CANCER RISK? (MEETING ABSTRACT).

Hirayama T
Epidemiology Division, National Cancer Center Research Institute, Tokyo, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

Daily intake of soybean paste soup was found to significantly reduce standardized mortality rates for gastric cancer in our ongoing large scale prospective study for 122,261 males and 142,857 females age 40 and above in 29 health center districts in Japan, 1966-78, the rates being 171.9, 210.2, 240.0 and 255.9 in males and 77.8, 85.3, 97.5 and 113.6 in females in daily, occasional, rare and non intakers respectively. These relationships remained significant when observed by smoking habit and by socio-economic status. Such risk reducing effect was also observed by case-control studies in the past both in ma les and females and in urban and rural areas. The observed beneficial effect could come from selected nutritious substances included in the paste, but it is also possible that this just reflects the effect of some other substance(s) closely associated with the intake of soybean paste soup such as green-yellow vegetables. (no Refs)

BIOCHEMICAL, MORPHOLOGICAL AND IMMUNOLOGICAL ASPECTS OF GI CARCINOGENESIS

46. CARCINOPLACENTAL ALKALINE PHOSPHATASE IN MALIGNANT AND PREMALIGNANT CONDITIONS OF THE HUMAN DIGESTIVE TRACT.

Skinner JM, Whitehead R
Dept. Pathology, Flinders Univ. South Australia, Bedford Park 5042, South Australia
Virchows Arch [Pathol Anat]; 394(1/2):109-118 1981

The presence of carcinoplacental alkaline phosphatase (CP Alk P) was demonstrated in the cells of malignant and premalignant states of the human stomach, colon and rectum using the immunoperoxidase technique. It was shown to be present in 7 out of 18 carcinomas of stomach and 7 of 17 cases of carcinoma of colon and rectum. In the putative premalignant states it was demonstrated in 4 of 15 cases of intestinal metaplasia associated with gastric carcinoma, and 9 of 12 tubulovillous adenomas of colon. However, it was also demonstrated in five of eight metaplastic polyps of colon which are neoplastic and in 9 of 17 cases of intestinal metaplasia not associated with cancer of the stomach. It was not seen in normal gastric mucosa and only faintly in 1 of 11 samples of normal colon. CP Alk P has been shown to be a specific marker of malignancy in a wide range of human cancers when studied in sera from patients or in tissue culture of tumor cells. In this study however, although a statistical difference exists between normal and diseased tissue the marker appears as frequently in non-neoplastic states. It is concluded that CP Alk P is, in tissues, a marker of proliferative activity in cells, rather than neoplastic or malignant change. In this respect it is similar in some respects to carcinoembryonic antigen, but not other markers of placental origin such as pregnancy specific beta, glycoprotein. (Author abstract) (20 Refs)

47. COMPARATIVE STUDY ON THE NUCLEAR DNA CONTENT OF LEIOMYOMA, LEIOMYOBLASTOMA AND LEIOMYOSARCOMA OF THE STOMACH AND SMALL INTESTINE.

Kimura O, Kaibara N, Tamura H, Nishidoi H, Okamoto T, Koga S (c/o Kaibara) The 1st Dept. Surgery, Tottori Univ. Sch. Medicine, 36-1-Nishimachi, Yonago 683, Japan
Jpn J Surg; 11(6):428-432 1981

Nuclear DNA contents in tumor cells of leiomyoma (LM), leiomyoblastoma (LB) and leiomyosarcoma (LS) of the stomach and small intestine were determined and the DNA distribution pattern and histopathological findings were evaluated. Five LM, four LB, and two LS of the stomach, and one LS of the small intestine were obtained at the time of gastrectomy, intestinal resection and biopsy. Nuclear DNA content was determined by staining the sections according to the Feulgen method. Three of five gastric LM had developed in the gastric corpus and two were located in the cardia. No ulcer formation of LM, except in one case, was noted. LB were located in the corpus and cardia. Ulcer formation was noted in two patients. LS were the largest in size, and ulcer formations were apparent in all patients. The mean DNA content for LM was 2.2-2.7 CC (CC= range distribution), 3.0-3.1 CC for LB, and 4.6-5.8 CC for LS. Peak DNA values were in the diploid area in LM and LB. Missing of peak value in LS indicated aneuploidy. A significant difference in nuclear DNA content exists among the tumors, and percentage of nuclei with DNA content 3 or 4x over the basic CC represent good indices for distinguishing between benign and malignant conditions. In differentiated types of LS is sometimes difficult to make histopathological distinction between LM and LB. Diagnosis of LS may be more accurate when more than 80% of the nuclei have DNA content values greater than 3x of basic nuclear content and when more than 50% exhibit values greater than 4x of basic content. (8 Refs)

48. HUMAN-TUMOR-DERIVED CELL LINES CONTAIN COMMON AND DIFFERENT TRANSFORMING GENES.

Perucho M, Goldfarb M, Shimizu K, Lama C, Fogh J, Wigler M
Cold Spring Harbor Lab., Cold Spring Harbor, NY, 11724
Cell; 27(3):467-476 1981

We have screened different cultured cell lines established from human tumors for the ability of their DNAs to induce transformed foci in NIH/3T3 cells. Based on restriction endonuclease digestions and the presence of human sequences in mouse transformants, we conclude that five of these human tumor cell lines contain a gene or genes capable of transforming mouse cells and that at least three different transforming genes are present in these five lines. Three cell lines, two derived from lung carcinomas and one derived from a colon carcinoma, transfer the same or closely related human genes. If these transforming genes are mediating the tumorigenic state of the human cells, then our results indicate that overlapping pathways leading to tumorigenesis may arise independently. (Author abstract) (32 Refs)

49. VARIOUS ISOZYME GENE EXPRESSION PATTERNS AMONG HUMAN COLORECTAL ADENOCARCINOMA CELL LINES AND TISSUES.

Rutzky LP, Siciliano MJ
Dept. Surgery, Univ. Texas Medical Sch. at Houston, Houston, TX, 77030
JNCI; 68(1):81-90 1982

Seven tissue-specific isozymes lactate dehydrogenases A and lactate dehydrogenase B (LDHA and LDHB), esterase B2 and esterase A4 (ESB2 and ESA4), creatine kinase B (CKB), and red blood cell and tissue forms of adenosine deaminase (ADA) were examined in the human adenocarcinoma cell line LS174T and its subclones grown under a wide variety of conditions. Strong expressions of ESB2, ESA4, and CKB were stable in all material studied, as was a greater expression of LDHA than of LDHB. ADA isozyme expression varied with culture conditions. Identical expression of the five stable isozymes was observed in six surgical specimens or normal bowel mucosa, white cell lines derived from normal mucosa varied in the expression of these isozymes. An additional 23 colorectal cell lines, derived from primary or metastatic adenocarcinomas in different stages of invasiveness and differentiation from 18 individuals, were verified as to their origin by genetic signature analysis and similarly studied for isozyme expression. These lines had different, yet stable, gene expression patterns similar to differences observed among six adenocarcinoma surgical specimens. These differences could not be related to the number of passages that the cell lines were in culture nor to the stages of the tumors at the time that the cell lines were initiated or surgical samples tested. Gene expression patterns in adenocarcinomas differed, these differences might have been due to the origin of colorectal adenocarcinomas from different cell types within a heterogeneous mucosa, and the colorectal cell lines studied represented appropriate models for colon cancer. (Author abstract) (53 Refs)

50. BIOLOGICAL CHARACTERIZATION OF LARGE BOWEL POLYPS BY MEANS OF FLOW CYTOPHOTOMETRY (MEETING ABSTRACT).

Jacobasch K, Weiss H, Wildner GP

Central Institute Cancer Research Academy Science, Berlin-Buch, E. Germany

UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Adenomas of the colon are known to be precursor lesions of adenocarcinoma. The frequency of dysplasia and invasive carcinomas in adenomas is related to the histological type and to the size of the adenoma. Nothing is known about the malignant potential of a particular adenoma. The aim of our investigation is to contribute to the biological characterization of large bowel polyps and to give the clinician a further parameter of classification of polyps and for his decision in which intervals follow up is to be done. Fifty large bowel adenomas removed by endoscopical polypectomy were investigated by flow cytophotometric analysis. Our results show, that the parameters DNA-distribution and percentage of cells in the cell cycle stages do not differ at various types of benign polyps. At some of the benign adenomas irregularily shaped S-phases and scattered or split 4C-Peaks were found. These changes are assumed to indicate malignant potential, since they are observed in some malignant polyps too. (no Refs)

51. HISTOLOGICAL DISTRIBUTION OF COLON ADENOMA; OBSERVATION OF EXPERIMENTAL COLON ADENOMA AND HUMAN FAMILIAL COLON ADENOMA (MEETING ABSTRACT).

Nakamura S, Kino I

Dept. Pathology, Hamamatsu Univ., Sch. Medicine, Hamamatsu-shi, Shizuoka Pref. 4 31-31, Japan

Program and Proceedings of the 15th Meeting of the Japanese Research Society for Cancer of the Colon and Rectum held in Kagoshima, Japan, 24 July, 1981. The Japanese Research Society for Cancer of the Colon and Rectum, Osaka Pref. 589, Japan, 66 pp., 1981.

The histological distribution of colon adenoma induced by 1,2-dimethylhydrazine in ICR mice was examined with complete serial sections, and it was shown that the adenomas were located on the upper layer of the mucosa, and began with a single tubular adenoma showing endophytic growth. The cell dynamics was examined by the use of autoradiography with 3H-thymidine, and reversal of the growing zone and spread of adenoma over the superficial epithelium were not observed. Further, in four cases of human familial colon adenoma also it was seen that the adenoma began with a single tubular adenoma, and microlesions which could be called 'keim' of adenoma were present. The keim was composed of atypical epithelial cells, was located in the middle to upper part of the existing tubule, and was seen as a form of budding in the existing tubule to the lamina propria. These results indicate that these keims bud in the growing zone of the lower part of the tubule, move upward and grow with tubular epithelium, and become single tubular adenomas in the superficial layer of the mucosa. (no Refs) (In JPN)

52. TUMOR-ASSOCIATED CHROMATIN ANTIGENS OF HUMAN COLON ADENOCARCINOMA CELL LINES HT-29 AND LOVO.

Duhl DM, Banjar Z, Briggs RC, Page DL, Hnilica LS

Dept. Biochemistry, Vanderbilt Univ. Sch. Medicine, Nashville, TN, 37232

Cancer Res; 42(2):594-600 1982

Antiserum to dehistonized chromatin from human colon adenocarcinoma cell line HT-29 was raised in rabbits and used for the immunodetection of colon tumor-associated nuclear antigens. Quantitative microcomplement-fixation studies indicated that the antiserum had reactivity similar to those of chromatins of two human colon adenocarcinoma cell lines (HT-29 and LoVo) and with nonneoplastic colon. Immunocytochemical localization showed the chromatin antigens to be evenly dispersed throughout the nucleus. Immunochemical staining of electrophoretically separated chromosomal proteins transferred to nitrocellulose sheets revealed several intensely staining antigens predominantly in the mol wt range of 62,000 to 75,000. When the antiserum was immunoabsorbed with nonneoplastic human colon chromatin, two antigens with mol wt of 67,000 and 92,000 were identified only with the tumor chromatins. Antiserum immunoabsorbed with either LoVo or HT-29 chromatin failed to show any immunoreactivity, suggesting that these tumor-associated proteins, or antigenic sites residing on these proteins, are identical in both colon tumor cell lines. (Author abstract) (43 Refs)

53. INDUCTION OF RAT COLONIC EPITHELIAL ORNITHINE DECARBOXYLASE (ODC) BY BILE SALTS, AND ITS ENHANCEMENT BY COLON CARCINOGENS PRETREATMENT (MEETING ABSTRACT).

Takano S, Akagi M, Bryan GT

Department of Surgery, Kumamoto University, Kumamoto, Japan

Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

A single intrarectal (ir) instillation of bile salts, presumptive colon promoters, results in a significant, early transient dose-response induction of rat colonic polyamine biosynthetic enzymes, ODC and S-adenosyl-L-methionine decarboxylase. Pretreatment by ir N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) or sc dimethylhydrazine (DMH) 1 wk before bile salt treatment enhanced and prolonged deoxycholate-induced ODC levels. This enhancement was dependent on pretreatment dose of MNNG, and was observed up to 3 mo after MNNG pretreatment. These data suggest that induced colonic ODC activity by bile salts may be related to colon carcinogenesis in a manner analogous to that shown to occur in mouse skin tumor systems. (no Refs)

54. EFFECTS OF DIETARY BRAN AND THE COLON CARCINOGEN 1,2-DIMETHYLHYDRAZINE ON A FECAL BETA-GLUCURONIDASE ACTIVITY IN MICE.

London JF, Clapp NK, Henke MA

Oak Ridge Graduate Sch. Biomedical Sciences, Univ. Tennessee, Oak Ridge, TN, 37830

Food Cosmet Toxicol; 19(6):707-711 1981

Daily variations in fecal beta-glucuronidase (BGLU) activity in BALB/c mice and variations in BGLU activity induced by different dietary brans and/or 1,2-dimethylhydrazine (DMH) were investigated. The effect of DMH on BGLU was significant. Three mo after DMH treatments, mice had persistently depressed BGLU activity compared to mice not treated with

DMH. BGLU activities of animals on control or wheat bran diets were 4-5x higher than the activities in animals on either soya-bean bran or corn-bran diets and differed significantly from them. Animals fed the corn-bran diet consistently had the lowest BGLU activities in fecal stream. No synergistic action of any combination of variables was noted. (63 Refs)

55. NEOPLASTIC PATHOLOGY OF THE STOMACH IN THE EARLY STAGE: PRELIMINARY STUDY (MEETING ABSTRACT).

Vernetti L, Giacchino P, Valletti A, Venturi GC, Giacchino L, Nicora E
Ospedali Galliera, Genoa, Italy
Medicina Domani Genova '81: Ulcera Peptica e Cancro Gastrico, April 23-24, 1981, Genoa, Italy. University of Genoa 126 pp., 1981.

In this paper we report certain results of a critical study of results obtained in gastric resections for neoplasms in their early stages. Our case series which consists of 35 patients includes: superficial cancerization of glandular epithelia 'superficial adenocarcinoma' (5 cases, 14.2%), marginal cancerization of gastric ulcers with or without infiltration (25 patients, 71.4%, all with a long history of stomach ulcer), and 'early cancer' intramucosal carcinomas (5 cases, 14.2%). Uniform treatment o f this heterogeneous group of neoplastic pathology is justified by the fact that it has as its common denominator earliness and superficiality of the lesion beyond the problem of etiopathogenesis, anatomopathology and nosology. Our patients' 5 yr survival was 78.8%; at 10 yr it was a little less (75.5%). Overall mortality secondary to neoplasm recurrence or metastasis, 8 cases (24.25%) occurred during the first 6 yr but primarily in the first 4 (7 cases). Considering that most of the deceased patients belonged to the group of stomach ulcer turned cancerous with infiltration of the stomach wall beyond the muscularis mucosae, proceeding on the basis of the considerations stated earlier, we have planned a comparative study of survival, on the one hand, and degree of morphologic differentiation and infiltration, on the other, for the near future. (no Refs) (In ITA)

PANCREATIC CARCINOGENESIS

56. ANTIGENS OF HUMAN PANCREATIC ADENOCARCINOMA CELLS DEFINED BY MURINE MONOCLONAL ANTIBODIES.

Metzgar RS, Gaillard MT, Levine SJ, Tuck FL, Bossen EH, Borowitz MJ
Dept. Microbiology and Immunology, Duke Univ. Medical Center, Durham, NC, 27710
Cancer Res; 42(2):601-608 1982

We have elicited and characterized the serological specificity of five murine monoclonal antibodies (DU-PAN-1, 2, 3, 4, and 5) to a human pancreatic tumor cell line, HPAF. The antibodies are not detecting HLA-associated antigens since all of the monoclonals failed to react with human lymphoid and myeloid cell lines and uncultured cells. All of the monoclonals except DU-PAN-5 reacted with four of five pancreatic tumor cell lines and two of two uncultured pancreatic tumors. An immunoperoxidase technique was used to determine the presence of the antigens detected by the monoclonal antibodies in frozen sections of tumor and adult and fetal normal tissues. DU-PAN-1 antigen was detected on pancreatic tumors, and a transitional cell carcinoma of the bladder, but was detected on no other adult or fetal normal tissues including pancreas. One of the antigens (DU-PAN-2) defined by the monoclonals was present on pancreatic ductal epithelial cells and showed a restricted distribution on tumor cells from some other carcinoma patients and on cells from certain fetal tissues. DU-PAN-3 antigen was present on adult and fetal pancreatic cells and certain tumor cells but could not be detected on cells of other fetal or adult normal tissues. DU-PAN-4 and DU-PAN-5 antigens have a more widespread distribution on normal or tumor cell types. (Author abstract) (9 Refs)

57. COFFEE AND CANCER OF THE PANCREAS.

Cuckle HS, Kinlen LJ
Radcliffe Infirmary, Univ. Oxford, Oxford OX2 6HE, England
Br J Cancer; 44(5):760-761 1981

The correlation between changes in pancreatic cancer and coffee consumption was established after allowing changes for lung-cancer mortality, using data from western Europe, Scandinavia, Japan, Australia, and the United States. Total correlation coefficients between changes in pancreatic cancer and coffee consumption and partial coefficients allowing for the effect of changes in smoking were 0.61 and 0.58, respectively, for males and 0.68 and 0.66, respectively, for females. Excluding Japan, the values were 0.14 and 0.33, respectively, for males and 0.15 and 0.15, respectively, for females. For countries other than Japan, the correlation coefficients for males were higher. (9 Refs)

58. ULTRASTRUCTURAL ANALYSIS OF PANCREATIC CARCINOGENESIS. IV. PSEUDODUCTULAR TRANSFORMATION OF ACINI IN THE HAMSTER PANCREAS DURING N-NITROSO-BIS(2-HYDROXYPROPYL)AMINE CARCINOGENESIS.

Flaks B, Moore MA, Flaks A
Dept. Pathology, Univ. Bristol Medical Sch., University Walk, Bristol, England
Carcinogenesis; 2(12):1241-1253 1981

Electron and high resolution light microscope studies were made of the pseudoductular structures that develop in the pancreas of the Syrian hamster during chronic treatment with the pancreatocarcinogen, N-nitroso-bis(2-hydroxypropyl)amine (BHP). These pseudoductules, which precede the development of tumors, arise from acini, whose cells undergo dedifferentiation by selective autophagy of their zymogen granules and granular endoplasmic reticulum. It is proposed that the pseudoductules develop into the ultrastructurally similar cystic foci that appear to be the immediate precursors of pancreatic tumors in this experimental model. The possibility is discussed that the acinar cells are the primary target for BHP carcinogenesis. (Author abstract) (36 Refs)

59. THE DIFFERENCE OF 3H-THYMIDINE UPTAKE AMONG 5 FU OR 5 FU COMBINED WITH NCS TREATED AND NOT TREATED GROUPS OF DHPN-INDUCED PANCREATIC CANCER IN HAMSTERS (MEETING ABSTRACT).

Miyazaki K
First Department of Surgery, Kyoto University School of Medicine, Kyoto, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

One of the most remarkable features of cancer cells is autochthonous increased proliferation. This experiment was done to clarify the increase of 3H-thymidine uptake in dinitrophenylhydrazine (DHPN) induced pancreatic cancer and its decrease by the therapeutic effect of 5-fluorouracil (5 FU) and Neocarcinostatin (NCS). Thirty-five female and 35 male hamsters were administered DHPN 500 mg/kg body wt, sc weekly and 5 females and 5 males vehicle only. After 13 wk, 20 females and 20 males were administered 5 FU 1 mg ip qod. In 10 females and 10 males 5 FU was combined with 2 mg NCS ip. Seventeen, 18 and 19 wk later, radioactivity ie cpm of 3H-thymidine/DNA concentration in DHPN-induced pancreatic cancer was revealed to be increased vs control pancreases by liquid scintillation spectrometry. Uptake of 3H-thymidine was decreased in the 5 FU group and most in the NCS group. (no Refs)

REVIEWS AND OTHER RELATED STUDIES

60. CARCINOMA OF THE COLON AND RECTUM (MEETING ABSTRACT).

Fisher E
No affiliation given
Current Concepts in Cancer Therapy, December 10-12, 1981, St Louis, Missouri Washington University School of Medicine; 1981

Colorectal carcinoma attributes to 14% of all deaths due to cancer in the United States. The peak incidence of this disease is in the seventh decade with 8% diagnosed before age forty. Certain disease definitely predispose to development of colorectal carcinoma; familial polyposis, Gardner's syndrome and vilous adenomas. In some cases, adenomatous polyps may be premalignant lesions. Colorectal carcinoma is more common in urbanized civilizations than in rural areas. It is felt that diets low in roughage and high in sugar may be carcinogenic by prolonging contact of fecal material with colonic mucosa and promoting action of neoplastic agents. Possible carcinogens could be formed from bile by bacterial growth or derived from foods. Seventy per cent of colorectal cancers are found in the distal colon and rectum. The most common site of metastasis is to regional lymph nodes. Lymph nodes are involved in over 90% of cases where carcinoma has spread through the bowel wall. In cases where the lesion is confined to the bowel wall, positive nodes are present in over 45% of the cases. Positive nodes are often found some distance from the primary site with intervening normal nodes. For this reason, long segments of colon are removed. The size of the primary tumor does not correlate well with either incidence of metastases or survival. Prognosis is fairly well predicted by the Dukes Classification and it can be used at the operating table as a guide to the proper operation. Final classification of the tumor is done after permanent histologic slides are examined. (no Refs)

61. IS COLON CANCER A DISEASE OF CIVILIZATION?.

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Div. Gastroenterology, Edgewater Hosp., 5700 N. Ashland Ave., Chicago, IL, 60660

Minerva Dietol Gastroenterol; 27(4):638-640 1981

Epidemiology of carcinoma of the colon (CC) is discussed. CC has become increasingly common in North America and Western Europe in the last 30 yr. These areas have higher income, a higher standard of living, and higher meat consumption. A diet rich in meat and associated animal fat increases the production of cholic acids. Feces have higher amounts of cholic acids and their degradation products, some of which are carcinogens. Constipation, another problem associated with a higher standard of living, increases the amount of time feces are in contact with intestinal walls. Japanese, Poles, and other Eastern Europeans, all from areas that are low in CC, become as prone to CC as the rest of the population after emigration to the United States. On the other hand, Seven Day Adventists living in Loma Linda, California and consuming vegetarian diets have a much lower CC rate than the rest of the population; the amount of cholic acids and their derivatives in their feces is much lower. Another factor associated with diet is the type of bacterial flora and enzymes active in the intestines (beta-glucuronidase, nitroreductase, azoreductase etc). Associated with these problems is increased intestinal diverticulosis. Current dietary recommendations are for decreased total calories, animal fat, and cholesterol, and increased vegetable fibers and unsaturated fats. (14 Refs) (In ITA)

☆ U. S. GOVERNMENT PRINTING OFFICE : 1982—361-847/119

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As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. ETHYLENE OXIDE (ETO): EVIDENCE OF CARCINOGENICITY.
Coene RF
National Inst. for Occupational Safety and Health, Cincinnati, OH
Vet Hum Toxicol; 23(6):439-443 1981

DIETARY FACTORS IN CARCINOGENESIS

2. NUTRITIONAL ASPECTS OF CANCER PREVENTION: AN OVERVIEW.
Silverman J
American Health Foundation, Naylor Dana Inst Disease Prevention, Valhalla, NY, 10595
J Am Vet Med Assoc; 179(12):1404-1409 1981

3. FORMATION OF N-NITROSO COMPOUNDS IN FOODS.
Gray JI
Dept. Food Science and Human Nutrition, Michigan State Univ., East Lansing, MI, 48824
ACS Symp Ser; 174():165-180 1981

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

4. LYMPHOMAS AND LEUKAEMIAS. PART 2: TROPICAL AMERICA.
Jimenez E
Hospital Nacional de Ninos 'Dr. Carlos Saenz Herrera', Apartado 1654, San Jose, Costa Rica
Clin Haematol; 10(3):894-915 1981

5. LYMPHOMAS AND LEUKAEMIAS. PART 1: TROPICAL AFRICA.
Olweny CL
Uganda Cancer Inst., P.O. Box 3935, Kampala, Uganda
Clin Haematol; 10(3):873-893 1981

6. MALIGNANT MELANOMA.
Creagan ET
Div. Medical Oncology, Mayo Clinic, Rochester, MN, 55905
Compr Ther; 7(12):36-44 1981

7. MELANOTIC TUMORS OF THE UVEA AND RETINA.
Schmitt H
Universitats-Augenklinik, Theodor-Stern-Kai 7, D-6000 Frankfurt am Main, W. Germany
Med Klin; 76(24):672-675 1981
In GER

CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

8. THE NATURAL HISTORY OF CARCINOGENESIS: IMPLICATIONS OF EXPERIMENTAL CARCINOGENESIS IN THE GENES'S OF HUMAN CANCER.
Pitot HC, Goldsworthy T, Moran S
McArdle Lab. for Cancer Res., Dept. Oncology, Medical Sch., Univ. Wisconsin, Madison, WI, 53706
J Supramol Struct Cell Biochem; 17(2):133-146 1981

9. CURRENT CONCEPTS AND CONTROVERSIES IN CHEMICAL CARCINOGENESIS.
Weinstein IB
Div. Environmental Sciences, Inst. Cancer Res., Columbia Univ. Coll. Physicians and Surgeons, New York, NY, 10032
J Supramol Struct Cell Biochem; 17(2):99-120 1981

VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

10. BURKITT'S LYMPHOMA.
Ambrus JL, Ambrus CM
Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
J Med; 12(6):385-413 1981

11. PRIMARY HEPATIC CARCINOMA.
Iosquin CJ
Catedra de Medicina Interna A, Facultad de Ciencas Medicas, La Plata, Argentina
Rev Fac Cienc Med La Plata; 4(2):27-31 1981
In SPA

METHODOLOGY IN CARCINOGENESIS RESEARCH

12. MUTAGENESIS AND CARCINOGENESIS TESTING IN VITRO.
Casto BC
Northrop Services, Incorporated, P.O. Box 12313, Research Triangle Park, NC, 277 09
Biotechnol Bioeng; 23(12):2659-2671 1981

OTHER REVIEWS IN CARCINOGENESIS

13. CANCER IN THE YEAR 2000. A REVIEW.
Saxen E
Suomen Syoparekisteri, Liisankatu 21 B, 00170 Helsinki 17, Finland
Duodecim; 97(20):1708-1716 1981
In FIN

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ORGAN SITE CARCINOGENESIS

Gastrointestinal Tract and Pancreas

SERIES CK09 No. 82/07

JULY, 1982

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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HE 20.3173/2:

PREVALENCE OF GI CANCER IN HUMAN POPULATIONS

1. CANCER INCIDENCE AND MORTALITY IN THE UNITED STATES, 1973-77.

Young JL, Percy CL, Asire AJ, Berg JW, Cusano MM, Gloeckler LA, Horm JW, Lourie WI, Pollack ES, Shambaugh EM

(c/o Berg) Dept. Pathology, Univ. Colorado Medical Sch., Denver, CO, 80262

Natl Cancer Inst Monogr; 57:1-187 1981

Data on cancer incidence and mortality in the United States between 1973 and 1977 are presented. Data are classified according to sex, race, age, and residence of the patients, anatomic site, and histologic type of cancer. For all areas, excluding Puerto Rico, the av annual age-adjusted incidence rates for all malignant neoplasms and for carcinoma in situ were 331.5 and 26.7 per 100,000, respectively. The most common primary sites of cancer were colon/rectum, breast, and lung, with age-adjusted incidence rates of 48.5%, 46.7%, and 46.7%, respectively. The three sites accounted for 42.7% of all malignant cancers. Seventy-eight percent of in situ lesions occurred in the female genital system. Av annual mortality due to malignant neoplasms for the total United States was 166.5. Of all cancer deaths, lung cancers accounted for 21.7%, colorectal 13.6%, and breast 9.2%. Considerable variation was noted in both incidence and mortality from cancer among various racial and ethnic groups. Generally males had higher cancer rates than females. Striking differences occured among the race-sex groups and geographic areas with respect to incidence of cancer by sites. An incidence-to-mortality ratio of 1.97 was obtained. Data is classified according to 304 specific anatomic sites. Distribution of the 8,968 non-Hodgkin's lymphomas is described in terms of anatomic site (24% were extra-nodal) and race. Of all malignant cancers, 51% were diagnosed in patients aged 65 yr and older. The median age for diagnosis of patients with malignant lesions was 65.4 yr compared with 37.1 yr for in situ lesions. Of all neoplasms, 34.7% were classified adenocarcinomas, 12.4% as squamous cell carcinomas, and 9.4% as duct adenocarcinomas. A comparison with previous data is presented. (14 Refs)

2. CANCER INCIDENCE AND MORTALITY IN METROPOLITAN DETROIT, 1973-77.

Swanson GM, Brennan MJ

Dept. Social Oncology, Michigan Cancer Foundation, 110 East Warren Ave., Detroit, MI, 48201

Natl Cancer Inst Monogr; 57:219-297 1981

Data on cancer incidence and mortality in metropolitan Detroit (1973-1977) are presented. Differences between data from Detroit and those obtained by the Surveillance, Epidemiology, and End Results (SEER) Program are described. Less disparity between blacks and whites occurs in incidence rates in Detroit than is seen for the total SEER population. The increase in mortality rates was greater for Detroit blacks than for blacks in all SEER areas. Cancer sites for which Detroit appears to differ considerably from the total SEER program include lung and bronchus, colon, female breast, and prostate gland. (no Refs)

3. CANCER INCIDENCE AND MORTALITY IN METROPOLITAN NEW ORLEANS, 1974-77.

Halperin ST, Wellbaecher RG, Correa P, Krementz ET

Louisiana Tumor Registry, 2-3-4 Loyola Building, Suite 1000, New Orleans, LA, 70112

Natl Cancer Inst Monogr; 57:409-487 1981

Cancer incidence and mortality in metropolitan New Orleans (1974-77) is discussed in terms of primary site, race, sex, and age. Both malignant tumors and in situ lesions are considered. New Orleans data show an overall high cancer incidence in blacks, mainly due to excessive rates for cancer of the lung, buccal cavity, esophagus, stomach, cervix, and prostate gland. For some cancers, including breast, ovary, bladder, and kidney cancers and the lymphoma-leukemia group, whites have a moderately excessive rate compared with blacks. Differences between New Orleans data and those obtained by the Surveillance, Epidemiology, and End Results Program are described. Particularly marked is the excess of respiratory cancer in New Orleans. (no Refs)

4. CANCER INCIDENCE AND MORTALITY IN NEW MEXICO, 1973-77.

Key CR

New Mexico Tumor Registry, 900 Camino de Salud NE, Albuquerque, NM, 87131

Natl Cancer Inst Monogr; 57:489-595 1981

Data on cancer incidence and mortality in New Mexico (1973-77) by primary site, sex, race, and age are presented. Data for Hispanics, Anglos, and Indians are compared. For all cancers and for the most common cancers, the Anglo population had incidence rates similar to those for whites in the Surveillance, Epidemiology, and End Results Program. Overall rates for Hispanic males and females were considerably lower than those for all whites. However, for some specific cancers, such as gallbladder, stomach, and cervix, the rates were much higher than for comparison populations. Although New Mexico's American Indians have low total cancer incidence rates, the rates for cancer of the gallbladder, stomach, and uterine cervix were even higher than among Hispanics. (no Refs)

5. CANCER INCIDENCE AND MORTALITY IN UTAH, 1973-77.

Lyon JL

Utah Cancer Registry, 540 Arapeen Drive, Room 204, Salt Lake City, UT, 84143

Natl Cancer Inst Monogr; 57:597-627 1981

Data on cancer incidence and mortality in Utah (1973-77) by age, sex, race, and primary site are presented. Both carcinomas and in situ lesions are considered. Utah has the lowest overall incidence of cancer for any of the Surveillance, Epidemiology, and End Results Program registries. The lower-than-expected incidence of cancer is attributed almost exclusively to the portion of the Utah population which is Mormon. Deficits noted for various cancer sites are heavily concentrated in those sites of the body associated with tobacco and/or alcohol use including the tongue, oral cavity, pharynx, larynx, esophagus, and urinary bladder (no Refs)

6. CANCER INCIDENCE AND MORTALITY IN PUERTO RICO, 1973-77.

Martinez I
Dept. Health, Cancer Control Program, Box 9342, Santurce, Puerto Rico, 00908
Natl Cancer Inst Monogr; 57:947-977 1981

Data on cancer incidence and mortality in Puerto Rico (1973-77) are presented by primary site and sex. Both malignant and in situ lesions are considered. Puerto Rico had a higher incidence of cancer of the mouth, hypopharynx, esophagus, stomach, and penis in comparison with findings for all Surveillance, Epidemiology, and End Results (SEER) Program areas. The incidence for all SEER areas, excluding Puerto Rico, was higher for cancers of the lip, colon, rectum, retroperitoneum, lung, bronchus, pleura, melanoma of skin, breast, corpus uteri, ovary, testis, urinary bladder, kidney, brain, endocrine glands, and lymphomas and leukemias. (no Refs)

7. EPIDEMIOLOGY OF THE MOST FREQUENTLY OCCURRING TUMORS OF THE DIGESTIVE SYSTEM.

Naujoks-Heinrich S, Dolle W
Abteilung Innere Medizin I, Universitatsklinik, Otfried-Muller-Strasse 10, D-7400 Tubingen, W. Germany
Internist (Berlin); 23(1):1-9 1982

The epidemiology of esophageal, gastric, and colorectal cancer is reviewed. These types of cancer are described with respect to incidence, variations in incidence between countries, age and sex distribution of patients, lethality, exogenous factors that increase the risk of cancer development, benign conditions associated with each, and genetic predisposition to cancer development. Exogenous factors that increase the risk of development of esophageal cancer include alcohol and tobacco use; among the benign conditions frequently associated with this type of cancer are achalasia, scleroderma, Plummer-Vinson syndrome, and benign esophageal stricture. Genetic aspects of gastric and colorectal cancer are examined with respect to studies of the incidence of these diseases in Japanese people living in Japan and emigrants of Japanese ancestry. Exogenous factors that increase the risk of developing gastric cancer include occupational exposure to coal dust and exposure to trace elements such as asbestos in drinking water. Pernicious anemia, gastric polyps, and ulcera ventriculi are among the benign conditions associated with this type of cancer. The role of diet in the development of colorectal cancer is emphasized; the relative significance of animal fats, vegetables, and fiber in the diet is considered. The general field of epidemiology is discussed with regard to methodologic problems, including variations between countries in diagnostic methods and criteria as well as problems in documentation. (52 Refs) (In GER)

8. MORTALITY TRENDS FOR STOMACH CANCER IN ENGLAND AND WALES.

Davies JM
Div. Epidemiology, Inst. Cancer Res., Clifton Ave., Sutton, Surrey SM2 5PX, England
Br J Cancer; 44(6):879-885 1981

Despite a decline in mortality rates since about 1931 stomach cancer remains a major cause of death in England and Wales. National death rates from 1916 to 1979 are presented by sex, age and two broad social-class groups covering manual and non-manual occupations. In both sexes the decline in rates has been most rapid in the young and has slowed progressively with advancing age. The rat io of male/female rates is currently 1.3 at ages 25-34, increases to a peak of 2.7 at ages 55-64 and then declines again but the pattern was different before 1931. Among both men and married women, rates are consistently higher in manual than in non-manual classes, but the difference is greater among men. Rates for men in non-manual occupations, and for both classes of married women, declined markedly between 1931 and 1951, but for male manual workers the decline was relatively slight until after 1951. (Author abstract) (18 Refs)

9. CANCER MORBIDITY IN NORTH-WESTERN INDUSTRIAL REGION OF THE SOVIET UNION.

Merabishvili VM, Serova LS
N. N. Petrov Res. Inst. Oncology, Leningrad, USSR
Vopr Onkol; 27(12):3-8 1981

Cancer morbidity in the North-Western region (NWR) of the European part of the Soviet Union is reported. The overall morbidity index for NWR exceeded that for USSR; increased morbidity was recorded for both the urban and rural populations. In 1975, the incidence (per 100,000 persons) of lung cancer, colonic cancer, stomach cancer, breast cancer, and cervical cancer was 30.2, 76.9, 57.7, 12.5, and 2.9, respectively. The decrease of morbidity indices was recorded for cervical cancer, compared with the increase of breast cancer morbidity. (3 Refs) (In RUS)

10. THE PREVALENCE OF POLYPS OF THE LARGE INTESTINE IN OSLO: AN AUTOPSY STUDY.

Vatn MH, Stalsberg H
Rikshopitalet, Oslo 1, Norway
Cancer; 49(4):819-825 1982

The colon and rectum were removed from 445 consecutive autopsies and examined for the presence of polypoid lesions under an illuminating magnifying lens. There were seven clinically undiagnosed carcinomas, 329 adenomas, 174 hyperplastic polyps, 59 mucosal tags, 34 other polypoid lesions, and 54 polyps in which no histologic diagnosis could be made. Adenomas were present in 34% of the men and 32% of the women. The adenoma prevalence rate increased smoothly with age in men, whereas the rate in women showed a biphasic variation with a peak at 50-59 years followed by a second increase after 70 years of age. The distribution of adenomas within the bowel showed a marked change with age, from a moderate left-sided predominance before 60 years of age to a marked right-sided predominance in patients over 80 years of age, particularly in men. Hyperplastic polyps were present in 27% of the men and 18% of the women. In men, their frequency and distribution within the bowel showed similar changes with age as were seen for the adenomas. In women, no such age-dependency was observed for hyperplastic polyps. Multiplicity of polyps increased with age and was more pronounced in men than in women. Adenomas in women tended to be larger, more atypical, and more villous than in men. A comparison with a similar study from Northern Norway showed no difference in the prevalence of adenomas in spite of a 70% higher incidence rate for colorectal cancer in Oslo. (Author abstract) (23 Refs)

11. PERNICIOUS ANEMIA AS A RISK FACTOR IN GASTRIC CANCER. THE EXTENT OF THE PROBLEM.

Eriksson S, Clase L, Moquist-Olsson I
Dept. Medicine and Pathology, Univ. Lund, Malmo General Hosp., Malmo, Sweden
Acta Med Scand; 210(6):481-484 1981

We have analyzed the prevalence of pernicious anemia (PA) in all patients with autopsy-verified gastric carcinoma (GC) registered during 1958-76 in a Swedish city, with one Department of Pathology serving approx 240,000 inhabitants and with a high autopsy frequency. The prevalence was compared to that in a reference group of 917 sex- and age-matched individuals without GC. PA was found in 19 persons, 2.1%, (7 males and 12 females) in the GC group and in 13 persons, 1.4%, (5 males and 8 females) in the reference group. This difference is not significant (p less than 0.15). After exclusion of individuals with PA known for less than 5 yr before death, the corresponding figures were 16 in the GC group against 8 in the control group. This difference is significant (p less than 0.05). Regarding individuals with a diagnosis of PA for greater than 10 or greater than 15 yr, the prevalence was twice as high in the GC as in the reference group. The differences were again insignificant (p less than 0.10) . PA as a risk factors for the development of GC has been overestimated, probably due to inadequate reference groups. Only 2% of all GCs are associated with PA. Large-scale preventive search for GC in PA patients is thus unjustified. (Author abstract) (10 Refs)

12. SPATIAL PATTERN OF PRIMARY LIVER CANCER COMPARED TO THAT OF OESOPHAGEAL CANCER IN GOLDMINERS FROM TRANSKEI, 1964-1979.

McGlashan ND, Harington JS, Bradshaw E

(c/o Harington) Cancer Res. Dept., National Cancer Association, P.O. Box 2000, Johannesburg 2000, South Africa

S Afr J Sci; 77(10):471-473 1981

The spatial pattern of primary liver cancer was compared to that of esophageal cancer in goldminers from Transkei; detailed geographic analysis of places of recruitment for cases of esophageal cancer revealed a significant similarity with the spatial pattern of Transkei residents, both male and female, who had not been absent while migrant laborers. (5 Refs)

13. CANCER MORBIDITY IN USSR IN 1979 (ANALYSIS OF MORBIDITY INDICES).

Napalkov NP, Merabishvili VM, Tserkovnyi GF, Preobrazhenskaia MN

No affiliation given

Vopr Onkol; 27(11):3-27 1981

Cancer morbidity indices in the Soviet Union are summarized. An overall intensive index for 1979 was 201.6 per 100,000. A total number of newly detected cancers exceeded 530,000. Cancer morbidity in urban population was by 21.8% greater than that in rural population. The increase of morbidity indices was recorded for rectal cancer, lung cancer in men, skin cancer, breast cancer, and lymphatic and hematopoietic neoplasms. The decrease of morbidity indices was recorded for lip cancer, stomach cancer, and cervical cancer. There was no changes in the morbidity indices for esophageal cancer and lung cancer in women. The growth of prevalence index was indicative of the efficacy of the system of of cancer detection and follow-up. The overall index of 1-yr mortality was 35.4%. Absolute number of patients who died of cancer reached 366,400. The decrease of mortality indices was recorded for stomach cancer and cervix cancer. The increase of mortality indices was recorded for cancers of the mouth, pharynx, esophagus, rectum, larynx, lungs, breast, and urinary organs. (12 Refs) (In RUS)

14. CHANGING DISEASE PATTERNS IN SOUTH AFRICA.

Walker AR

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S Afr Med J; 61(4):126-129 1982

Progressive changes in disease patterns are identifiable when comparing: (i) past with present populations; (ii) rural with urban dwellers; and (iii) emigrants from developing (to Western) countries with non-emigrants. In contexts of underprivilege the main causes of death are infections (with or without malnutrition), particularly in the young. In contexts of prosperity the main causes are degenerative diseases - coronary heart disease (CHD), cancer, 'strokes', diabetes, and, not least, alcohol-related diseases. Whether viewed historically or cross-sectionally, South African populations (Black, Indian, Colored and White), provide valuable evidence of the effects of changes in diet and lifestyle on patterns of sickness and death. South African Whites have reached an all-time peak in mortality from CHD. Indians now experience high morbidity and mortality rates from CHD and diabetes, diseases actually known to Indian physicians before the time of Hippocrates. The Colored population is experiencing greatly increased mortality rates from a variety of cancers - esophageal, cervical, stomach, and lung. Blacks, especially in urban areas, have much reduced child mortalities. While Black adults still have low mortalities from bowel diseases and CHD, they have high mortalities from hypertension-linked diseases and from infections. Greater characterization of these populations and their subdivisions should provide additional knowledge of the factors which promote or inhibit changes in disease patterns. (Author abstract) (46 Refs)

15. POSSIBLE APPLICATIONS OF MUTAGENESIS TESTING IN CANCER EPIDEMIOLOGY.

Haenszel W, Magee PN, Tannenbaum SR, Correa P, Hill MJ, Reddy BS, Stemmermann GN, Bruce WR, Lipkin M, Nigro ND, Venitt S, Goldin BR, Hirayama T, Archer MC, Balis ME, Keefer LK, Goldman P, Balish E, Strobel HW, Eisenbrand G

Biometry-Epidemiology Program, Univ. Illinois, Sch. Public Health, Chicago, IL, 60616

Banbury Rep; 7:431-446 1981

Epidemiological applications of mutagenesis studies for stomach and large bowel cancer are reviewed. A cohort study of stomach cancer in a high-risk population in Colombia has been proposed; positive tests for mutagenicity in gastric juice samples were found only when nitrites were present. High-risk North American populations are suitable for bowel cancer studies. Linkage of pathology, fecal chemistry, and mutagenesis data will improve screening for large-bowel cancer and help to elucidate the pathways leading to large-bowel cancer. (20 Refs)

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN GI CARCINOGENESIS

16. MORTALITY PATTERNS AMONG WORKERS IN THREE TEXAS OIL REFINERIES.

Thomas TL, Waxweiler RJ, Moure-Eraso R, Itaya S, Fraumeni JF
Occupational Studies Section, Environmental Epidemiology Branch, NCI, Bethesda, MD, 20205
JOM; 24(2):135-141 1982

The cause-specific mortality experience of 2,509 active and retired members of the Oil, Chemical, and Atomic Workers International Union (OCAW) who worked at three oil refineries in the Beaumont/Port Arthur area of Texas was examined to determine whether there might be unusual patterns of fatal disease related to workplace exposures. Deaths that occurred between 1943 and 1979 were identified from membership records of the OCAW headquarters in Denver and from the records of Union locals in Texas which represent workers at the three refineries. Death certificates were obtained from state vital records offices for the decedents. Cause-specific Proportionate Mortality Ratios (PMRs) were calculated using the mortality experience of the US general population as a standard. Excess mortality from stomach cancer occurred among active union members who worked at Refinery A and among active and retired members who worked at Refineries B and C. PMRs for leukemia, multiple myeloma, and other lymphomas were elevated, especially among retired workers. Relative frequencies of brain tumor deaths were significantly elevated among active members at all three refineries and slightly elevated among retirees at Refineries A and C. Findings suggest that oil refinery workers may have elevated risks of these cancers and indicate that more definitive studies are necessary. (Author abstract) (22 Refs)

17. SMOKING AS RISK FACTOR FOR DIFFERENT FORMS OF CANCER AMONG 26,000 MEN AND WOMEN IN NORWAY. MATCHING OF THE GROUP OF SMOKERS WITH THE CANCER REGISTRY OVER A 12-YEAR PERIOD.

Lund E, Zeiner-Henriksen T
Kreftregisteret, Montebello, Oslo 3, Norway
Tidsskr Nor Laegeforen; 101(34-36):1937-1940 1981

The cancer risk due to smoking was studied among 11,979 men and 13,998 women born between 1895 and 1929 on the basis of data in the Norwegian Cancer Registry for the period 1966-1977. A total of 1,815 cases of cancer were registered for this group during the studied period. Nonsmokers accounted for 22.4% among men and 76.5% among women, ex-smokers for 21.7% and 4.2%, current smokers for 55.4% and 19.1%, and the smoking habits of 0.5% of the men and of 0.2% of the women are unknown. The age-adjusted relative risk (relative to nonsmokers) per 1,000 men was found to be 4.8 for lung cancer and 2.3 for cancer of the urinary bladder and urethra. For women, the relative risk was found to be 1.9 for lung cancer, 1.5 for cancer of the urinary bladder and urethra and 1.3% for cancer of the uterine cervix. The relative risk for all smokers was found to be 1.4 for lip cancer (men), 7.5 for stomach cancer (men), 4.4 for colon cancer (men), 0.9 for larynx cancer, 9.2 (men) and 1.7 (women) for lung cancer, 3.3 for cancer of the uterine cervix, 12.4 for prostate cancer, 3.7 (men) and 1.2 (women) for cancer of the urinary bladder and urethra, 4.8 (men) and 3.4 (women) for lymphoma and leukemia. Significant difference between smokers and nonsmokers was found with respect to laryngeal cancer (men), esophageal cancer (men), cancer of the liver and bile ducts (women) and carcinoma of the uterine cervix as well. The risk of cancer of the upper respiratory passages are higher for pipe smokers than for cigarette smokers, while cigarette smokers had higher risk of lung cancer than pipe smokers. The cancer risk was found to be lower among ex-smokers than current smokers, and it increased with cigarette consumption. (17 Refs) (In NOR)

DIETARY AND DIGESTIVE FACTORS IN GI CARCINOGENESIS

18. BILE ACIDS IN COLORECTAL CARCINOGENESIS.

Hill MJ, Montesano R, Bruce WR, Correa P, Lipkin M, Goldman P, Tannenbaum SR, Reddy BS
Bacterial Metabolism Res. Lab., Central Public Health Lab., London NW9 5DX, England
Banbury Rep; 7:365-380 1981

A mechanism for the adenoma-carcinoma sequence in the large bowel is proposed and discussed with respect to various mutagens that have been described in fecal extracts and to bile acid metabolites. One genetic factor and at least three environmental factors are involved in the postulated mechanism. Persons who are adenoma-prone will develop colorectal adenomas only when exposed to a factor whose concentration depends on environmental conditions. Exposure to a further factor results in an increase in the size of the adenomas, and exposure to a third factor causes dysplastic changes to occur and progress, eventually leading to malignancy. (29 Refs)

19. BILE SALTS AND OTHER CONSTITUENTS OF THE COLON AS TUMOR PROMOTERS.

Reddy BS, Tannenbaum SR, Montesano R, Correa P, Haenszel W, Wattenberg LW
Div. Nutrition, American Health Foundation, Naylor Dana Inst. for Disease Prevention, Valhalla, NY, 10595
Banbury Rep; 7:345-363 1981

The mechanisms by which dietary components increase the risk of developing colon cancer are reviewed and etiologic factors in large-bowel carcinogenesis are discussed. Dietary fat and fiber affect fecal bile acid excretion, which may then affect carcinogenesis. Cholesterol and its metabolites are mutagenic and have colon-tumor-promoting activity. Fecal mutagens and comutagens in high- and low-risk populations for colon cancer were studied. (63 Refs)

20. INTAKE, FORMATION, AND RELEASE OF MUTAGENS BY MAN.

Stich HF, Rosin MP, San RH, Wu CH, Powrie WD, Van Soest PJ, Wattenberg LW, Watson JD, Tannenbaum SR, Wilkins TD, Magee PN, Bruce WR
Environmental Carcinogenesis Unit, British Columbia Cancer Res. Centre, Vancouver, British Columbia V5Z 1L3, Canada
Banbury Rep; 7:247-266 1981

The incidence of stomach cancer was high in Japan during the Edo period of its history, when foodstuffs were not contaminated by industrial or agricultural chemicals. During the past several decades, when the uses of these chemicals increased in Japan and elsewhere, the incidences of cancer of the stomach, esophagus, and mouth in Japan declined steadily. Many classes of compounds occurring in fresh, cooked, and stored foodstuffs have been identified as mutagens. The use of food additives, pesticides, and herbicides will undoubtedly add to the mutagenic load of foodstuffs. The available evidence raises several questions: whether foodstuffs comprise the major source of mutagens (and, by implication, carcinogens) in the human body; why the cancer frequency is so low, despite this daily intake of mutagens; and why DNA repair-deficient patients (eg, those with xeroderma pigmentosum) develop skin cancers at an early age but lack a comparable frequency of gastrointestinal cancers. It is difficult to discard the idea that people always ingest enough carcinogens to produce neoplastic cells, but that the occurrence of this event is enhanced or suppressed by genetic factors, whose role may be greater than hitherto assumed. If mutational events are involved at all in tumor initiation, they may not be the types of events detected by the in vitro bioassays now used. The number of different mutagens in food products, digested foods, and feces is evidently very large. The genetic damage in somatic cells may be the product of the actions of many mutagens rather than of one predominating substance. (31 Refs)

21. ISOLATION OF A MUTAGEN PRODUCED IN THE HUMAN COLON BY BACTERIAL ACTION.

Wilkins TD, Lederman M, Van Tassell RL, Wattenberg LW, Wilkins TD, Bruce WR, Goldin BR
Dept. Anaerobic Microbiology, Virginia Polytechnic Inst. and State Univ., Blacksburg, VA, 24061
Banbury Rep; 7:205-214 1981

The feces of about 30% of North Americans contain mutagenic activity in the Ames assay, and greater than 90% of this mutagenicity is due to one substance. The isolation and purification of this substance are described. Evidence indicating its production by colonic bacteria is presented. Dietary supplementation with ascorbic acid or vitamin E (3 wk each) did not affect the fecal concentration of the mutagen in three donors. Two of these donors were a married couple who ate almost every meal together, but the wife consistently excreted much more mutagen than her husband. The daily variation in mutagen excretion was completely random. The mutagen was stable under strictly anaerobic conditions and strongly fluorescent under long-wave UV light. It was extremely sensitive to oxidation, decomposing (in a manner similar to catalytic lipid peroxidation) to a substance which was neither mutagenic nor fluorescent. The mutagen acted directly on Salmonella strains TA98 and TA100 in both its crude and purified forms. The presence of microsomal enzymes reduced its mutagenicity. Since the substance was not mutagenic for the parent strain of TA98 (TA1538), it may act by causing base-pair substitutions. This substance is not the only mutagenic compound present in human feces, but it is the most active substance in the Ames test. (10 Refs)

22. NITROSATION REACTIONS OF STOMACH MUCOSAL TISSUE OF THE HUMAN AND DOG.

Rice S, Ichinotsubo D, Stemmerman G, Hayashi T, Palumbo N, Sylvester S, Nomura A, Mower H, Goldman P, Mower HF, Tannenbaum SR, Goldin BR, Fine DH, Hill MJ, Reddy BS, Hecht SS, Newmark H
Dept. Chemistry, Univ. Hawaii, Honolulu, HI, 96817
Banbury Rep; 7:185-203 1981

Gastric mucosa specimens from patients who had received hydroxyzine-HCl (HZ), diazepam (DP) and cimetidine before gastrectomy, were assayed for mutagens in Salmonella strains TA98, TA100, TA1535, and TA1537. Mutagenic activity was identified in 21/65 specimens. High pressure liquid chromatographic assays identified the mutagens as nitrosated metabolites of HZ and DP. The enzymes required to metabolize these agents were never found simultaneously in the same specimen. The antral mucosa seemed to be unique among human gastrointestinal tissues in its ability to produce nitrosated metabolites of HZ and DP. No metabolites of fenantyl were found in the human tissues. Specimens of gastric antral mucosa from dogs (without prior drug treatment) contained several mutagens, mostly of the TA98 direct-acting type, in about 20% of cases. A similar number of mutagens occurred in the lower colon mucosa. The enzymes of the canine antral mucosa were capable of nitrosating HZ, DP, and fenantyl. No mutagenic metabolites were identified when human or canine antral mucosa was incubated with cimetidine in vitro, or in the antrum of a dog treated with dinitrosocimetidine 24 hr previously, but chemically synthesized nitrosated analogs of cimetidine showed mutagenic activity in all Salmonella strains except TA98. No component of the diet or environment is known to be nitrosated by the enzyme system discovered in the human antral mucosa, but the experiments with canine tissues suggested that some dietary or environmental components probably do interact with the nitrosative metabolism of the gastric or colonic mucosa. (4 Refs)

23. MUTAGENS IN EXTRACTS OF GASTROINTESTINAL MUCOSA.

Stemmermann GN, Mower H, Rice S, Ichinotsubo D, Tomiyasu L, Hayashi T, Nomura A, Mandel M
Pathology Dept., Kuakini Medical Center, Honolulu, HI, 96817
Banbury Rep; 7:175-183 1981

Mucosal specimens from 60 resected stomachs (31 from stomach cancer patients) and 25 colons (11 from colon cancer patients) were assayed for the presence of mutagenic compounds in Salmonella typhimurium TA98 and TA100. The specimens for assay were not grossly involved with cancer. Nitrosated TA98 mutagens were identified in 32/60 stomach specimens, mostly from the antrum. Both sex and age seemed to play a role in determining whether the antral tissues contained mutagens. The TA98 mutagens derived from the antral mucosa were generally nitrosated derivatives of diazepam, hydroxyzine, and cimetidine (which had been used in anesthesia), which does not mean that these agents are carcinogenic in the stomach or any other organ. However, their presence in the stomach serves as a model for the in vivo generation of nitrosated mutagenic compounds. The metabolic process can occur in the absence of dietary nitrite, provided that the gastric epithelium is exposed to any one of a wide variety of amide precursors. These observations support the epidemiologic findings of an inverse correlation between stomach cancer and the intake of foods containing substances (eg, ascorbic acid and vitamin E) blocking the nitrosation process. The intestinal specimens yielded a wide variety of TA98 and TA100 mutagens, which were not characterized chemically. Some of these mutagens seemed to favor specific sites in the colon. (6 Refs)

24. FAT, FIBER, AND OTHER MODIFIERS OF INTESTINAL CARCINOGENESIS: A STRATEGY FOR PREVENTION.

Nigro ND, Van Soest PJ, Kingston DG, Bruce WR, Tannenbaum SR, Hill MJ
Dept. Surgery, Sch. Medicine, Wayne State Univ., Detroit, MI, 48201
Banbury Rep; 7:83-93 1981

Published reports on the effects of diet on intestinal carcinogenesis in rats (a process requiring a carcinogen) suggest that the influence of dietary fiber is much smaller than the influence of dietary fat. A high-fiber diet shows a protective effect only when the dietary fat level is low. The effect of a high-fat diet may be mediated through the presence of large amounts of steroids in the large intestine, interacting with the bacterial flora. Epidemiologic data on colorectal cancer in populations having different dietary habits tend to support the results of animal experiments. Further studies are needed to define the relative proportions of dietary fat and fiber for the optimal prevention of colorectal cancer. If only the levels of dietary fat and fiber are changed, it is clear that the changes must be substantial; one report suggests that a 50% reduction in fat and the consumption of bran would be required to reduce the incidence of colorectal cancer in a high-incidence population. Such drastic changes are unlikely to be accepted by the general population or even persons at high risk. It is suggested that a diet containing bran, a less stringently reduced amount of fat, and vegetables inducing benzopyrene hydroxylase in the large intestine (including cabbage, cauliflower, broccoli, and brussels sprouts) may be more acceptable, at least by persons at high risk of colorectal cancer. (28 Refs)

25. IMPLICATIONS OF DIETARY FIBER BREAKDOWN IN THE HUMAN COLON.

Cummings JH, Stephen AM, Branch WJ
MRC Dunn Clinical Nutrition Centre, Old Addenbrookes Hosp., Cambridge, CB2 IQE, England
Banbury Rep; 7:71-81 1981

Metabolism of fiber in the colon and implications for human carcinogenesis are reviewed. Possible hypotheses for the mechanism of the protective effect can be obtained from examining data on the dominant effects of fiber on colorectal function. Dietary fiber is extensively degraded in the colon, leading to production of short-chain fatty acids (butyrate) which may affect colonic cell function. Fiber breakdown also stimulates microbial growth in the colon, leading to increased bulk of the colonic content, faster transit rate, and rerouting of nitrogen metabolism. Fiber fermentation in the colon diverts nitrogen metabolism from ammonia formation (ammonia is more toxic to normal cells than transformed cells) to bacterial protein synthesis. If endogenous nitrite synthesis occurs in the human colon, it may arise from the oxidation of ammonia. The optimum pH for bacterial nitrification in pure cultures and natural ecosystems is alkaline (7.0-8.5). A metabolic consequence of a high-fiber diet may be reducing the colonic pH to a level unfavorable to nitrite synthesis from ammonia, leading to a reduced formation of N-nitroso compounds. The urinary excretion of protein metabolites other than ammonia declines when wheat fiber is added to the diet, showing another change in the direction of nitrogen metabolism in the colon. Any or all these events may be important in protection from colorectal cancer. (56 Refs)

26. FACTORS THAT AFFECT INTESTINAL BACTERIAL ACTIVITY: IMPLICATIONS FOR COLON CARCINOGENESIS.

Goldin BR, Lombardi P, Mayhew J, Gorbach SL, Tannenbaum SR, Wilkins TD, Reddy BS, Goldman P, Hill DH, Montesano R, Magee PN, Strobel HW
Dept. Medicine, Infectious Disease Services, Tufts-New England Medical Center, Boston, MA, 02111
Banbury Rep; 7:41-57 1981

Several experiments in male Fischer rats showed significant dietary effect on fecal beta-glucuronidase (B-Gase), nitroreductase (NRase), and azoreductase (AzRase) activities. Diets containing high levels of beef protein or beef fat were associated with a significant increase in these enzymes. The metabolic conversion of 2-nitronaphthalene (2-NN) or 2-naphthylamine-beta-D-glucuronide to 2-naphthylamine (an index of NRase activity) was significantly higher in beef-fed rats than in grain-fed controls. Dietary supplementation with Lactobacillus acidophilus, tetracycline, or erythromycin reduced fecal enzyme activities in the meat-fed rats to those in controls. The mutagenicity of 2-NN in a NRase-negative Salmonella strain was enhanced in the presence of liver microsomes only by a fecal extract containing NRase activity. Significant dietary effects on fecal enzyme activity were also observed in American adults (20-35 yr old). Lacto-vegetarians and strict vegetarians showed lower fecal B-Gase, NRase, AzRase, and 7-alpha-dehydroxylase activities than omnivores. No major differences were noted between the two vegetarian groups. Dietary supplementation with Lactobacillus caused decreases in fecal B-Gase, NRase, and AzRase activities in omnivores. The enzyme activities returned to baseline values after the supplementation was stopped. The high-animal protein and high-animal fat diets, which are associated with an increased risk of colorectal cancer, caused an increase in bacterial enzymes capable of generating carcinogens in the colon in the rats. The similar association between dietary habits and fecal enzyme activities in humans may provide a partial explanation for the strong positive correlation between daily beef and fat consumption and the incidence of colorectal cancer. (11 Refs)

27. PROPERTIES OF A MUTAGEN ISOLATED FROM FECES.

Bruce WR, Varghese AJ, Land PC, Krepinsky JJ, Montesano R, Wilkins TD, Van Soest PJ, Goldin BR, Reddy BS, Kingstn DG, Tannenbaum ST, Balis E, Watson JD, Mower HF
Ontario Cancer Inst., Toronto, Ontario, M4X 1K9, Canada
Banbury Rep; 7:227-238 1981

A mutagen, with strong activity on Salmonella strain TA100 without metabolic activation, was detectable (greater than 200 revertants/g) in freeze-dried feces from 4/12 healthy subjects and 4/7 patients previously operated upon for rectal cancer who were not on medication at time of study. High mutagen levels (greater than 800 revertants/g) were detected in one normal subject and one cancer patient. Mutagenicity was strongly correlated with UV absorption of the substance. The UV spectrum of the mutagen resembled that of a polyene antibiotic (filipin) but its nuclear magnetic resonance spectrum did not. The available data indicate at least two hydroxyl groups but no carboxyl or benzoyl groups in the molecule. (8 Refs)

28. SOME FACTORS INFLUENCING THE ECOLOGY OF GUT FERMENTATION IN MAN.

Van Soest PJ, Hill MJ, Wattenberg LW
Div. Nutritional Sciences and Dept. Animal Science, Cornell Univ., Ithaca, NY, 14853
Banbury Rep; 7:61-69 1981

In an 80-day experiment, 24 young men were fed a low-fiber basal diet (meat, eggs, mashed potatoes, and white bread) supplemented by high-fiber bread made with coarse of fine bran, cabbage powder, or wood cellulose (max fiber level, 40 g/day). The effects of the dietary fiber on digestive function varied from one fiber type to another. Particle size, hydration capacity, and fermentability were more important than the actual chemical constitution of the fiber source. A significant negative correlation was noted between the intestinal passage rate and fiber digestion. The efficiency of metabolic conversion from fermentable fiber to fecal nitrogen was greatest with coarse bran, followed by cabbage, fine bran, and cellulose. The results suggested that metabolism by colonic microorganisms and their net systems might create a metabolic sink, in which potentially toxic substances are incorporated into the microbial cellular mass. Increasing the size of the sink could become a means of detoxification by colonic microflora, since their non-carbohydrate requirements for cellular growth must be scavenged from the intestinal environment. Nitrogenous substances bound in the microbial cells are excreted in the metabolic fecal organic matter. The role of the colonic microflora as related to the intestinal environment and health may vary according to intestinal ecology and substrate availability. The nitrogen requirement of the intestinal microflora may vary from an ammonia- and amine-producing fermentation (oversupply of nitrogen) to a nitrogen-utilizing situation (insufficient supply) in which urea, ammonia, and perhaps other hazardous substances are utilized in the microbial cell synthesis. (13 Refs)

29. GASTROINTESTINAL CANCER: ENDOGENOUS FACTORS.

Bruce WR, Correa P, Lipkin M, Tannenbaum SR, Wilkins TD
Ontario Cancer Inst., Toronto, M4X 1K9, Canada
Banbury Rep 7: 468 pp., 1981.

The role of diet in cancer was examined. Sessions on gastrointestinal microbiology (microbiological considerations in experimental studies, effect of diet on human fecal flora, metabolism of xenobiotics by intestinal flora, and intestinal bacterial activity and carcinogenesis), fiber (ecology of gut fermentation in man, dietary fiber breakdown in the human colon role of fat, fiber, and other modifiers of intestinal carcinogenesis in cancer prevention), host response to carcinogens (risk factor profiles for individuals at increased risk for colon cancer, fecal mutagens and colorectal polyps, enzymes of normal, premalignant, and malignant colonic cells, role of cytochrome P-450 in colon response xenobiotics, inhibitors of gastrointestinal neoplasia, colonic activation of carcinogens), mutagens (in ext racts of gastrointestinal mucosa, nitrosation in stomach mucosal tissue of humans and dogs, isolation of mutagens produced in the human colon by bacterial action, structural studies and properties of mutagens isolated from human feces, bacterial fluctuation tests of mutagenic activity in human feces, intake, formation, and release of mutagens by man), N-nitroso compounds (endogenous formation of N-nitroso compounds, analysis of human biological specimens for nitrosamines, block nitrosamine formation using ascorbic acid and alpha-tocopherol, distribution and metabolism of nitrate and nitrite in rats, analysis of nitrate, nitrite, and nitrosamines in human feces, metabolism of nitrate), bile acids and other lipids (bile salts as tumor promoters, bile acids in colorectal carcinogenesis, and analysis of feces for benzopyrene after consumption of charcoal-broiled beef) and epidemiology and design of future studies (epidemiologic tests of hypothesis relating diet and cancer, large-scale cohort study of diet and selected digestive system cancers, and possible application of mutagenesis testing to cancer epidemiology). (716 Refs)

30. CANCER AND NUTRITION.

Betzler M
Chirurgische Univ.-Klinik, Heideberg, W. Germany
MMW; 124(2):21 1982

Selected aspects of the relationship between nutrition and cancer in humans are considered. Among the topics discussed are the role of diet in the etiology of certain types of cancer (eg, colon cancer), the clinical observation that many cancer patients are malnourished, the effect of nutritional status on the outcome of treatment, types of nutritional therapy for reversing cancer-related malnutrition, and the possibility that diet alone may have a prophylactic or therapeutic benefit in cancer development. (3 Refs) (In GER)

31. SHOULD WE EAT MORE FIBRE?

Stephen AM
Dunn Clinical Nutrition Centre, Addenbrookes Hosp., Trumpington St., Cambridge CB2 1QE, England
J Hum Nutr; 35(6):403-414 1981

Various aspects of the role of dietary fiber in health are discussed: epidemiological studies, effects of fiber on fecal weight, diverticular disease, colon cancer, ischemic heart disease, and the possibility of the recommendation of a standard fiber intake. Outline of a diet fed to volunteers, containing 40 g dietary fiber/day, is presented. The type of fiber to be recommended is discussed. (62 Refs)

32. CANCER AND DIET: SLACKENING PRUDENCE.

Froissart A
No affiliation given
Vivre; (233):4-9 1981

The value of dietary moderation in cancer prevention has been observed in Mormons. Although encouraged, natural foods may also contain carcinogenic agents, such as aflatoxins. Frequent ingestion of barbecued foods is discouraged because of the hydrocarbons produced when food is braised or smoked. Without many additives, much of the food consumed would be difficult to handle or too expensive. Additives are discussed in relation to dose, use, and associated cancer risks. Colonic, prostate, and breast cancer may be related to excess fat consumption. Epidemiological, animal, and cellular studies may be used to determine the carcinogenicity of chemical agents. Dietary excess and cancer are discussed. (no Refs) (In FRE)

OTHER ETIOLOGIC FACTORS IN GI CARCINOGENESIS

33. ALCOHOL AND CANCER.

MacSween RN
Univ. Dept. Pathology, Western Infirmary, Glasgow, Scotland
Br Med Bull; 38(1):31-33 1982

Epidemiologic and experimental studies are reviewed. Heavy alcohol consumption is assessed as a prime carcinogen of the esophagus and the mouth, a contributor of some type to carcinogenesis of the pharynx and larynx, and a cause of primary hepatocellular carcinoma in conjunction with hepatic cirrhosis. Associations with cancer of other portions of the gastrointestinal tract, the breast, thyroid, kidney, and bladder are equivocal. The actual mode of action is not known; possibilities are discussed. (30 Refs)

34. DEVELOPMENT OF RISK FACTOR PROFILES FOR INDIVIDUALS WITH INCREASED SUSCEPTIBILITY TO CANCER OF THE LARGE INTESTINE.

Lipkin M, Nordlicht N, Nigro ND, Wogan GN, Montesano R, Venitt S, Bruce WR, Archer MC, Wilkins TD
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Banbury Rep; 7:97-118 1981

Several populations at high risk of colorectal cancer (CRC) have been registered at Memorial Hospital, including asymptomatic persons and spouses: hereditary polyposis syndromes; site-specific CRC without polyposis; familial multiple cancers inducing CRC; and CRC patients with a second primary malignancy and a family history of CRC, cancer other than CRC, or no cancer. The registry also includes data on families having 41 cancer-free members over at least two generations. In familial CRC, the age at CRC onset differs significantly from the age at CRC onset in the general population. An attempt is being made to identify persons at high risk of CRC who are destined to develop CRC. The phenotypic characteristics collected into the 'risk profile' for patients with familial polyposis include the percentage of 3H-thymidine-labeled epithelial cells in the upper third of the colonic crypts in random biopsy specimens of flat colonic mucosa; the carcinoembryonic antigen content of colonic lavage specimens; mixed lymphocyte reactivity to allogeneic stimuli; the distribution of normal and abnormal actin concentrations in cultured cutaneous fibroblasts; and fecal concentrations of undegraded cholesterol and 7-alpha-dehydroxylase. A systematic analysis of the effects of stress on these parameters has also been started. Other risk factor profiles for other CRC risk groups are being formulated. (39 Refs)

35. PATHOLOGICAL EFFECTS OF LOW DOSES. LOW LINEAR TRANSFER ENERGY RAYS.

Dousset M
7, rue de la Gruerie, F 9190 Gif-sur Yvette, France
J Radiol; 62(11):556-560 1981

Somatic and genetic effects of low doses of low linear transfer energy are discussed in view of the diagnostic and therapeutic use of radiation. Prospective and retrospective studies relating radiation dose and effects are described. Findings on individuals exposed to irradiation at Hiroshima and Nagasaki are presented. With low dose radiation, there appears to be a curvilinear relationship between dose and effect with no threshold phenomenon. In experimental animals, irradiation prior to nidation results in the loss of the fertilized egg due to lack of implantation. During the first 35 days of human pregnancy, irradiation can result in malformations in the embryo. Fetal exposure to irradiation has been shown to increase the incidence of malignant disease. Radiation doses of greater than 100 rads can cause growth retardation among children irradiated prior to age 6 yr. An increased incidence of thyroid cancer has been observed among children less than 10 yr old exposed to low dose radiation. Adult exposure to radiation has been related to leukemia and cancers of the breast, thyroid, respiratory tract, bone, and digestive tract. Genetic effects of radiation are discussed. Male germ cells seem to be more sensitive to radiation than those of females. Germinal cells show varying sensitivities to radiation. (28 Refs) (In FRE)

INDUCTION OF GI CARCINOGENESIS IN ANIMALS

36. STUDIES ON EXPERIMENTAL COLON TUMORIGENESIS IN RATS 1. STRAIN DIFFERENCES IN INCIDENCE, LOCATION AND TUMOR TYPES OF 1,2-DIMETHYLHYDRAZINE-INDUCED TUMORS.

Naito Y
Res. Inst. for Nuclear Medicine and Biology, Hiroshima Univ., Hiroshima, Japan
Hiroshima J Med Sci; 30(4):355-362 1981

Susceptibility to 1,2-dimethylhydrazine (DMH), a direct acting carcinogen, in rats with a family history of spontaneous colon tumors (WF/O rats) and in Long Evans (LE) rats was investigated. WF/O and LE rats were divided into a treated group who received 20 mg/kg DMH for 20 wk, and a non-treated control group. Tumorous and non-tumorous sections of the gastrointestinal tract were examined following sacrifice at 10, 15, 20, and 25 wk. Wt gain in treated groups of WF/O and LE rats was similar, however animals with intestinal tumors showed a marked wt loss, diarrhea, or abdominal distension regardless of strains or sexes. Crude colon tumor incidence in WF/O and LE rats was 17/25 and 21/21, respectively. The av number of tumors per rat in WF/O and LE strains were 2.5 and 6.1, respectively. Both crude incidence and the av number of tumors/rat were higher in males than in females. Histologic examination revealed a higher number of colon adenomas in LE rats (41/128 tumors) than WF/O rats (6/42 tumors). Colon carcinoma incidence was higher in WF/O rats (35/42 tumors) than in LE rats (62/128 tumors). LE rats had the majority of tumors (59/128) in the descending colon, while WF/O rat tumors occurred primarily in the ascending colon (19/42). Seven cases of metastases from poorly differentiated adenocarcinomas was found in 18 WF/O rats. Seven cases of metastases (5 from poorly differentiated adenocarcinomas) were found in 21 LE rats. Contrary to expectation, this investigation has shown that WF/O rats were less susceptible to DMH than LE rats. (30 Refs)

37. ENZYMATIC, HEMATOLOGICAL AND HISTOLOGICAL STUDIES DURING CARCINOGENESIS OF THE LARGE INTESTINE IN RATS UNDER THE EFFECT OF N-METHYL-N'-NITRO-N-NITROSOGUANIDINE.

Przewlocki T, Chlap Z, Czosnek-Dabros E, Szot W
Zaklad Patofizjologii, Instytut Patologii AM, ul. Grzegorzecka 16, 31-531 Krakow, Poland
Patol Pol; 32(2):199-212 1981

The effects of N-methyl-N'-nitro-N-nitrosoguanidine (MNNG; 0.25% aqueous soln) administered as an enema for 7 wk, on enzymatic, hematological and histological characteristics were studied in 64 female Wistar WAG rats during carcinogenesis. Thirty-six other rats served as untreated controls. MNNG did not cause any significant changes in the hematological parameters before the appearance of tumors, but cystic degeneration of the liver was seen in some animals. Changes in the activities of some plasma enzymes were found during the intensive development of the tumors of the colon. The gamma-glutamyl transpeptidase and aspartate transaminase activities increased, and the cholinesterase activity decreased compared with the controls. Among the hepatic enzymes, aspartate transaminase and activity was increased in rats with hepatic cysts between wk 40-60. The alkaline phosphatase activities in the serum and liver showed no abnormal changes compared with the controls. The intensity of the enzymatic disturbances was correlated with the stage of development of the adenomas and adenocarcinomas of the colon. (43 Refs) (In POL)

38. MICROBIOLOGICAL CONSIDERATIONS IN INTERPRETATION OF DATA OBTAINED WITH EXPERIMENTAL ANIMALS.

Wilkins TD
Dept. Anaerobic Microbiology, Virginia Polytechnic Inst. and State Univ., Blacksburg, VA, 24061
Banbury Rep; 7:3-9 1981

The intestinal flora of rodents differs greatly from that of humans. The rodent forestomach is lined with lactobacilli, which may interact with any drug given po. Metabolically active yeasts line the secreting portion of the stomach. Large numbers of fecal bacteria may also be present, despite efforts to prevent coprophagy. The upper small intestine harbors an unusual filamentous bacterium which is poorly understood. These bacteria become attached to the host cell membranes. The first segment of the filament is modified into a specialized attachment cell that actually inserts into the host cell membrane to form intracellular bodies which are released and begin to multiply after they attach to new host cells. The terminal ileum harbors a large population of microorganisms, not closely associated with the mucosa, which metabolize oxidized compounds. Laboratory rats and mice have a small cecum because a laboratory diet provides enough nutrients whereas the cecum of wild rodents is large and harbors microorganisms that ferment complex polysaccharides of plant origin. The cecal and colonic flora of rodents consist largely of large fusiform organisms (mainly clostridia), which are not found in the human colon. Most of these species have not yet been described or named. Major dietary changes have little influence on the intestinal flora of humans, whereas dietary manipulation or starvation can cause drastic changes in the intestinal flora of rats and mice. Investigators studying dietary effects on colonic carcinogenesis in rodents should bear these differences in mind. (16 Refs)

39. CARCINOGENICITY TEST OF QUERCETIN AND RUTIN IN GOLDEN HAMSTERS BY ORAL ADMINISTRATION.

Morino K, Matsukura N, Kawachi T, Ohgaki H, Sugimura T, Hirono I
Biochemistry Div., Natl. Cancer Center Res. Inst., 5-1-1, Tsukiji, Chuo-ku, Tokyo 104, Japan
Carcinogenesis; 3(1):93-97 1982

Quercetin and its glycoside, rutin were tested for carcinogenicity in non-inbred golden hamsters of both sexes. In Experiment I, 10% quercetin, 10% rutin, or control diet was given to animals for 735 days. In this experiment, tumors appeared mainly in the forestomach, but the incidence was not statistically different among the three groups. Quercetin and rutin were not carcinogenic under these conditions. In Experiment II, Group 1 was given 4% quercetin diet for 709 days. Group 2 was given 1% quercetin diet for 351 days and then the basal diet for 350 days. Group 3 was given 1% quercetin diet and then 1% croton oil diet and Group 4 was given the basal diet followed by 1% croton oil diet, for the same periods as Group 2. Group 5 was given the basal diet for 701 days. In Experiment II, papillomas of the forestomach appeared in Groups 1, 2, and 5, and papillomatosis in Group 3 and 4. There were no statistical differences among experimental groups and respective controls. Thus, quercetin was not carcinogenic when given at the concentrations of 4% and 1%; even with the administration of 1% croton oil after 1% quercetin, there was no increase in tumor incidence. (Author abstract) (33 Refs)

40. TUMORIGENESIS WITH 1,1-DIALLYLHYDRAZINE IN MICE.

Toth B, Nagel D, Raha C
Eppley Inst. for Res. in Cancer, Univ. Nebraska Medical Center, Omaha, NE, 68105
Anticancer Res; 1(5):259-262 1981

The carcinogenicity of 1,1-diallylhydrazine (DAH) given to Swiss albino mice in drinking water for life was investigated. Fifty female and 50 male 6-wk-old mice received DAH in drinking water as a 0.03125% soln (av daily intake of DAH was 2.0 mg for females and 2.35 mg for males). Controls were 100 male and 100 female mice given tap water. Treatment reduced survival of both sexes when compared with controls. Lung tumors developed in 38 (76%) treated females and 38 (76%) treated males, and in 25 (25%) untreated females and 26 (26%) untreated males. Forestomach tumors developed in 7 (14%) treated females and 17 (34%) treated males, and in 4 (4%) untreated females. Histopathologically, the lung tumors were adenomas and adenocarcinomas and the forestomach tumors were squamous cell papillomas and carcinomas. The relative carcinogenic potencies of other disubstituted allylhydrazines are discussed. The tumorigenic potency of these compounds was strongly dependent on the nature of the alkyl substituents. (26 Refs)

41. INVESTIGATION OF THE TUMORIGENIC RESPONSE TO BENZO(A)PYRENE IN AQUEOUS CAFFEINE SOLUTION APPLIED ORALLY TO SPRAGUE-DAWLEY RATS.

Brune H, Deutsch-Wenzel RP, Habs M, Ivankovic S, Schmahl D

Biologisches Laboratorium, Vaselinwerk, Worthdamm 13-27, D-2000 Hamburg 11, W. Germany

J Cancer Res Clin Oncol; 102(2):153-157 1981

In a lifetime experiment benzo(a)pyrene (B(a)P) was administered to Sprague-Dawley rats either as an admixture to the diet or by gavage in an aqueous 1.5% caffeine soln. Dissolved benzo(a)pyrene induced more tumors of the forestomach than undissolved benzo(a)pyrene. The 1.5% caffeine soln (annual dose 27 g/kg) did not exert any carcinogenic activity under the conditions of this bioassay. (Author abstract) (17 Refs)

MECHANISMS AND MODIFICATIONS OF GI CARCINOGENESIS

42. INHIBITORS OF GASTROINTESTINAL NEOPLASIA.

Wattenberg LW, Lipkin M, Goldin BR, Tannenbaum SR, Magee PN, Balish E

Dept. Lab. Medicine and Pathology, Univ. Minnesota Medical Sch., Minneapolis, MN, 55455

Banbury Rep; 7:153-165 1981

Chemical carcinogenesis in the mouse forestomach is inhibited by a wide variety of agents, including phenols, lactones, disulfiram (DSM) and derivatives, aromatic isothiocyanates, indoles, and sodium cyanate. Intestinal carcinogenesis in rats and mice is inhibited by DSM and related compounds, butylated hydroxyanisole, butylated hydroxytoluene, vitamin E, and selenium salts. Many plant materials consumed by humans contain quercetin, which induces intestinal and bladder tumors in rats and may be the carcinogenic component of bracken fern. The addition of phenothiazine to the diet can inhibit the action of quercetin in mice. The role of intestinal microflora in the production or activation of chemical carcinogens requires further investigation. If the microflora are shown to be involved in intestinal carcinogenesis in humans, antibiotics acting on the intestinal microflora might have a protective effect against intestinal carcinogenesis. Many inhibitors of carcinogenesis have been discovered, often on the basis of empirical work. Some of these inhibitors have the advantage of very low toxicity. (36 Refs)

43. INHIBITORY EFFECTS OF SOME NEW RETINOIDS ON CARCINOGENESIS.

Cai H, Zhang J, Cui X
Chemical Etiology Lab., Cancer Res. Inst., Chinese Acad. Medical Sciences, Beijing, People's Republic of China
Yaoxue Xuebao; 16(9):648-653 1981

Retinoic acid has been shown to have an inhibitory effect on the chemically induced cancerous transformation of the squamous epithelium of the murine forestomach. However, due to its toxic side effects, this agent cannot be used clinically. Derivatives of retinoic acid that are less toxic but still possess activity against neoplastic transformation of the murine forestomach are described. Female Swiss mice were used. Of nine retinoic acid derivatives tested, five exhibited significant inhibitory effects on neoplastic transformation, with N-(4-ethoxycarbophenyl) retinamide (RI) particularly active. The effects of RI were reproducible and no toxicity was observed at the therapeutic dosage (1.1 x 10(-4) M/kg); even high doses (up to 6x the therapeutic dose) did not produce hypervitaminosis A, whereas retinoic acid at comparable doses produced marked hypervitaminosis A. One of the active derivatives caused marked inhibition of DNA synthesis in epithelial cells of the murine forestomach, as shown by autoradiography using tritium-labeled thymidine. (13 Refs) (In CHI)

44. CANCER AND BEHAVIOR: CONJUGATED EFFECTS OF METHYL NITROSOUREA (MNU) AND CONDITIONED EMOTIONAL RESPONSE (CER) ON EXECUTION OF A PROGRAM OF VARIABLE INTERVAL (VI) AND ON DEVELOPMENT OF NEOPLASIAS IN RATS.

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Facultad de Patologia, Universidad de Santo Tomas, Bogota, Colombia
Rev Latinoam Psicol; 13(3):375-401 1981

Of 12 male Wistar rats trained in a program of variable interval until they reached a stable state, 3 received methylnitrosourea (MNU: in 3 different doses), 6 received conditioned emotional response (CER) and MNU (in three different doses), 1 received saline soln, and 2 received CER and saline soln. Total rate of response was proportional to the dosage of MNU. Rats which received CER before MNU developed only medullary neoplasia (medulloblastoma or spongioblastoma), showed less cellular immunity to tumors and more development of neoplasia. Temporal discrimination of subjects, motivation, effects of CER and MNU and their interaction were analyzed. Location of neoplasia was spinal medulla (5), peripheral nervous system (2), and gastrointestinal mucosa (2). Types of tumors observed were medulloblastoma (2), spongioblastoma (3), neurinoma (2), and intestinal adenocarcinoma (2). (54 Refs) (In SPA)

45. TROPHIC EFFECTS OF GASTRIN ON COLORECTAL NEOPLASMS IN THE RAT.

McGregor DB, Jones RD, Karlin DA, Romsdahl MM
Dept. Surgery, Univ. Nevada - Reno, 1000 Locust St., Reno, NV, 89520
Ann Surg; 195(2):219-223 1982

This study was designed to determine the effect of gastrin on colorectal neoplasms in the rat. Multiple colon and rectal cancers were induced in each of 57 rats with methylazoxymethanol. Animals were randomly assigned to groups: (1) antral exclusion, (2) antrectomy, (3) sham, or (4) sham with subsequent pentagastrin injections. Resulting tumors were analyzed for concentration and synthesis of DNA, RNA, and protein. The number of tumors per rat and distribution of tumors within the colons did not vary among groups. Antrectomy did not alter the gastrin level, and tumors developing in these animals did not differ from those of sham controls. Antral exclusion markedly raised serum gastrin levels. Both chronic endogenous hypergastrinemia and administration of exogenous pentagastrin significantly increased tumor synthesis and concentration of DNA, RNA, and protein. We conclude that gastrin exerts a trophic effect on colorectal neoplasms in rats. This biological phenomenon suggests a tumor regulatory role for the hormone. (Author abstract) (11 Refs)

BIOCHEMICAL, MORPHOLOGICAL AND IMMUNOLOGICAL ASPECTS OF GI CARCINOGENESIS

46. METABOLISM OF NITRATE.

Tannenbaum SR, Green L, Balish E, Fine DH, Van Soest PJ, Bruce ER, Goldman P, Magee PN
Dept. Nutrition and Food Science, Massachusetts Inst. Technology, Cambridge, MA, 02139
Banbury Rep; 7:331-341 1981

Metabolism studies of nitrate in man and rodents are reviewed. Since 15NO3-was found in the feces of the germfree rat and [15N]urea in the urine of the conventional rat, a major portion of the nitrate that does not appear in the urine must enter the colon. In the germfree rat, the nitrate remained unmetabolized and was recovered in the feces. In the conventional rat, the nitrate was reduced to NH4+, converted to urea, and excreted in urine. Excess synthesis of nitrate was observed in men fed a low-nitrate diet. In man, an oral dose of nitrate was cleared effectively from the body within 36-48 hr. (9 Refs)

47. DISTRIBUTION AND METABOLISM OF NITRATE AND NITRITE IN RATS.

Balish E, Witter JP, Gatley SJ, Lipkin M, Reddy BS, Tannenbaum SR, Van Soest PJ, Magee PN
Dept. Surgery, Univ. Wisconsin Medical Sch., Madison, WI, 53706
Banbury Rep; 7:305-319 1981

Tissue distributions of nitrite (NO2) and nitrate (NO3) were studied in germfree (GF) and conventional (CV) Sprague-Dawley rats of both sexes in several feeding experiments. In some experiments, the supplementary NO2 or NO3 (1,000 ppm) in drinking water or given by gavage, was labeled with 13N. Bacteria were apparently responsible for the reduction of NO3 to NO2, because NO2 was not detected in the tissues of NO3-fed GF rats. Both ions were detected in the gastrointestinal (GI) tracts of GF rats fed water supplemented with either ion. The ions were less readily detected in the GI tracts of CV rats fed the same amounts of the ions. The 13N-labeling studies showed that the ions were distributed throughout the GI tracts of CV rats. The GI flora probably metabolized the ingested ions to compounds which could not be identified as NO2 or NO3. Whether these metabolites were harmless or harmful could not be determined by the methods used. The 13N data also showed that NO3 was secreted into the GI tract at many sites (saliva, bile, pancreatic and cecal secretions, etc), often from areas harboring a complex microbial flora. This NO3 secretion was enhanced at sites of trauma, tissue damage, or infection. These data showed the important role of the normal GI microflora in the distribution and metabolism of ingested

NO3. The composition of the flora could dictate the types of NO3 metabolites formed. Urinary NO3 excretion was greater in the GF rats than in CV rats fed the same amount of NO3. The reasons for this difference were not clear. (30 Refs)

48. TISSUE-SPECIFICITY OF N-NITROSODIBUTYLAMINE METABOLISM IN SPRAGUE-DAWLEY RATS.

Brittebo EB, Tjalve H
Dept. Toxicology, Univ. Uppsala, Box 573, S-751 23 Uppsala, Sweden
Chem Biol Interact; 38(2):231-242 1982

The distribution and metabolism of N-[14C]nitrosodibutylamine were studied in Sprague-Dawley rats. The results indicated that in addition to the liver, metabolism of the substance occurred in the nasal mucosa, the lung and the esophagus. Metyrapone and diethyldithiocarbamate reduced the production of 14CO2 from N-[14C]nitrosodibutylamine by all these tissues. There was no indication of metabolic capacity in the urinary bladder or the kidney. The results fit with the assumption that tumors of the urinary tract are induced by metabolites reaching these tissues via the urine. Besides the liver, the esophagus and the lung are target tissues for the carcinogenicity of N-nitrosodibutylamine in Sprague-Dawley rats and in these tissues the local formation of reactive metabolites may play a role in the pathogenesis of N-nitrosodibutylamine-induced lesions. (Author abstract) (21 Refs)

49. ENZYMES OF NORMAL, PREMALIGNANT, AND MALIGNANT COLONIC CELLS.

Balis ME, Higgins PJ, Salser JS, Stemmerman GN, Magee PN, Wattenberg LW
Dept. Cell Metabolism and Cell Biochemistry, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Banbury Rep; 7:129-139 1981

The villus and crypt cells of rat small intestine contained two different forms of adenosine deaminase (AD) and adenine phosphoribosyltransferase (APRT). The APRTs of normal and neoplastic rat colonic mucosa showed similar properties. Normal colonic mucosa showed predominantly one form of AD, but colonic tumors induced by methylazoxymethanol showed two distinct forms. The ADs of human colonic mucosa and colonic cancer were also distinctive. The tumor AD was smaller than that of normal tissue and was also immunologically distinct. In rat colon, ornithine decarboxylase (ODC) activity was about the same as in liver and only 1-2% that of the small intestine. Carcinogens caused a marked increase in the ODC activity of the target tissue: acetylaminofluorene in the liver, and dimethylhydrazine (DMH) in the colon. Thymidine kinase (TK) activity of the intestine was much higher in the fetal rat than in young or mature rats. After the administration of a colonic carcinogen (DMH), the colonic TK activity increased to levels resembling the fetal TK activity. Assays using rabbit antisera demonstrated two types of TK in normal human intestine, representing the flat mucosa and the crypts. A rabbit antibody against TK from human term placenta cross-reacted against cells from a number of tumor types, including abnormal cervical cells in Papanicolaou smears and colon carcinoma cells. This antibody also reacted with skin fibroblasts from patients with familial colonic polyposis. The specificity of the TK antibody for a variety of tumor types was greatly reduced by preabsorbing the rabbit antiserum with normal human colon extracts. (11 Refs)

50. THE INFLUENCE OF ANDROGENS, ANTI-ANDROGENS, AND CASTRATION ON CELL PROLIFERATION IN THE JEJUNAL AND COLONIC CRYPT EPITHELIA, AND IN DIMETHYLHYDRAZINE-INDUCED ADENOCARCINOMA OF RAT COLON.

Tutton PJ, Barkla DH
Dept. Anatomy, Monash Univ., Clayton, 3168, Australia
Virchows Arch [Cell Pathol]; 38(3):351-355 1982

Androgenic hormones have previously been shown to promote cell proliferation in the small intestine of rat and androgen receptors have been demonstrated in carcinomata of the large intestine of rat. In this study the influence of testosterone and of castration on epithelial cell proliferation in the small intestine, the large intestine and in dimethylhydrazine-induced colonic tumors is compared. Cell proliferation in the small intestine and in colonic tumors was accelerated by testosterone treatment, and cell proliferation in colonic tumors, but not in the small intestine, was retarded following castration. Cell proliferation in colonic tumors was also inhibited by the anti-androgenic drug, Flutamide. Testosterone and castration each failed to influence cell proliferation in the colonic crypt epithelium of both normal and carcinogen-treated animals. (Author abstract) (22 Refs)

PANCREATIC CARCINOGENESIS

51. SUBSEQUENT CANCER RISK IN THE INCIDENCE COHORT OF ROCHESTER, MINNESOTA, RESIDENTS WITH DIABETES MELLITUS.

Ragozzino M, Melton LJ, Chu CP, Palumbo PJ
(c/o Melton) Dept. Medical Statistics and Epidemiology, Mayo Clinic and Mayo Foundation, Rochester, MN
J Chronic Dis; 35(1):13-19 1982

Subsequent cancer incidence was determined in the population-based incidence cohort of Rochester, Minnesota residents diagnosed with diabetes mellitus between 1945 and 1969. The relative risk of having cancer, excluding cervical and nonmelanoma skin cancers, was not significantly increased following the diagnosis of diabetes mellitus. The potential biases of increased medical surveillance among diabetics and exacerbation of subclinical diabetes by occult malignancy did not appear to be important except in the case of subsequent pancreatic cancer. (Author abstract) (32 Refs)

52. REACTIONS OF VINYL CHLORIDE WITH RNA AND DNA OF VARIOUS MOUSE TISSUES IN VIVO.

Bergman K
Toxicology Lab., Natl. Food Admin., Box 622, S-751 26 Uppsala, Sweden
Arch Toxicol; 49(2):117-129 1982

The irreversible binding of 14C-vinyl chloride metabolites to RNA and DNA of mouse brain, lung, liver, kidney, spleen, pancreas, and testes after a single ip injection has been studied. Hydrolysates of nucleic acids from selected organs were separated on Aminex A6 for quantitation of alkylation products. Radioactivity in nucleic acids was registered in all of the studied organs with the exception of brain. RNA from spleen, pancreas and liver, and DNA from spleen and liver contained the highest amounts of radioactivity. In nucleic acids from spleen and pancreas, both organs of high metabolic activity, the entire radioactivity was found metabolically incorporated as C1-fragments. In RNA of kidney and liver, a large part of the radioactivity was also present as incorporated C1-fragments, but 3,N4-ethenocytidine (in kidney) as well as 1,N6-ethenoadenosine and 1,N6-ethenoadenine (in kidney and liver) were identified as alkylation products. In liver DNA, incorporation of C1-fragments was insignificant, indicating different interactions of vinyl chloride metabolites (C1-fragments and alkylating products) with RNA and DNA. The elution profiles of radioactivity in hydrolysates of liver DNA were dominated by an alkylation product of unknown structure (probably a derivative of deoxyguanosine). Possibly, 1,N6-ethenodeoxyadenosine and 1,N6-ethenoadenine were also present in liver DNA. The results are consistent with the ability of viny chloride to act as a multipotent carcinogen by alkylation of DNA in several tissues. (Author abstract) (45 Refs)

53. COFFEE CONSUMPTION AND PANCREATIC CANCER: TEMPORAL AND SPATIAL CORRELATION.

Benarde MA, Weiss W
Dept. Community Medicine and Environmental Health, Hahnemann Univ. Health Sciences, Philadelphia, PA, 19102
Br Med J; 284(6313):400-402 1982

An examination of available data on per capita consumption of coffee and pancreatic cancer mortality in the United States since 1950 shows a temporal association. A rise and fall in coffee consumption was followed by a rise and fall in the incidence of pancreatic cancer with roughly a 10-yr lag. Nevertheless, there were inconsistencies in this relationship by sex and race. An unimpressive spatial relationship was also found between the consumption of coffee and pancreatic cancer mortality in 13 countries. While this relationship suggests an association, major inconsistencies cast doubt on the possibilities that it is one of cause and effect. This may be due to confounding, particularly by cigarette smoking. The association between cigarette smoking and cancer of the pancreas is much more consistent with a casual relationship. (Author abstract) (25 Refs)

54. HYPERPLASTIC, PRENEOPLASTIC AND NEOPLASTIC LESIONS FOUND IN 83 HUMAN PANCREASES.

Pour PM, Sayed S, Sayed G
Dept. Pathology, Pharmaceutical Div., Preclinical Res., Sandoz Ltd., CH-4002 Basle, Switzerland
Am J Clin Pathol; 77(2):137-152 1982

A thorough histologic examination of the pancreas was performed on autopsy material from 83 military veterans aged 35-88 yr. Hyperplastic, preneoplastic and neoplastic alterations were recorded by severity, multiplicity, location, and age. From this material, two patients had clinically known primary, and three had secondary (metastatic), pancreatic cancer. The following occult malignant lesions were found: two early cancers (one adenocarcinoma and one adenosquamous cell carcinoma), one ductal carcinoma in situ and seven ductular carcinomas in situ. Among patients with ductular carcinoma in situ, three had pancreatic cancer and the remaining four had cancers of other sites (ethmoid, ear, colon, prostate). One patient who was clinically diagnosed as having lung cancer with selective metastases to the pancreas was found to have pancreatic adenosquamous cell carcinoma with lung metastases. Hence, the incidence of neoplastic exocrine lesions was around 10%. In addition, hyperplasia of the ductal and ductular epithelium (in 57% and 39% of the patients, respectively), squamous cell metaplasia of the ductules (in 48% of the cases), as well as endocrine tumors (islet cell adenoma, 10%; mixed ductular-insular adenoma, 3%) were found. Most lesions occurred in the pancreatic head, a few in the tail. These data and other reports lead to the conclusion that, first, the overall incidence of pancreatic cancer appears to be higher than previously reported. Malignant lesions seem to remain clinically occult, either because patients die of other diseases or because of the significantly long latency between premalignant lesions and clinically recognizable invasive cancer. Second, the ductular cells appear to be the progenitor cells of a variety of tumor types, including squamous cell cancer and islet cell tumors, as in the authors' experimental model. (Author abstract) (89 Refs)

REVIEWS AND OTHER RELATED STUDIES

55. THE SMOKING-INDUCED EPIDEMIC.

Doll R
Green Coll. Oxford, Oxford, England
Can J Public Health; 72(6):372-381 1981

Review of smoking-induced diseases and influence of smoking on cancer is presented. Harmful effects of smoking are demonstrated by the results of the large follow-up studies of men with defined smoking habits that have been carried out in many countries. Results of the studies are presented showing the mortality in regular cigarette smokers, standardized for age relative to that in life-long non-smokers. Causes of death for which smoking is responsible include cancers of the mouth, tongue, oropharynx, esophagus, larynx, lung, bladder, possibly the kidney, and probably the pancreas, chronic bronchitis and emphysema, pulmonary heart disease, myocardial infarction, aortic aneurysm, and a wide variety of other vascular diseases. Data on mortality from lung cancer by sex, mortality of regular cigarette smokers relative to non-smokers for women, characteristics of smokers by age, sex ratio of mortality rates in British doctors, relative risk of death by cause in non-smoking women by smoking habit of husband, incidence of lung cancer and vitamin A consumption, relative risks of developing various cancers in relation to serum retinol levels, and mortality of cigarette smoking by type smoked are presented. Mortality from lung cancer in women who are non-smokers is increased if they are married to men who smoke suggesting that the health of non-smokers is liable to be damaged by other people's smoke in public places. After confirmation of the new evidence smoking will then cease to be matter of concern only to the individual and his own family and will have to be classed together with other atmospheric pollution. (42 Refs)

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NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. AN EVALUATION OF THE GENETIC TOXICITY OF EPICHLORHYDRIN. A REPORT OF AN EXPERT GROUP OF THE INTERNATIONAL COMMISSION FOR PROTECTION AGAINST ENVIRONMENTAL MUTAGENS AND CARCINOGENS.

Sram RJ, Tomatis L, Bridges BA, Clemmesen J
(c/o Lohman), Medical Biological Lab. TNO, P.O. Box 45, 2280 AA Rijswijk, The Netherlands
Mutat Res; 87(3):299-319 1981

2. ETHYLENE DIBROMIDE (EDB). (REVISED).

NIOSH Document Development Branch
Robert A. Taft Lab., National Inst. Occupational Safety and Health, 4676 Columbia Parkway, Cincinnati, OH, 45226
Curr Intell Bull NIOSH (37): 13 pp., 1981.

3. CHEMICAL CARCINOGENESIS AND SMOKING.

Farber E
Dept. Pathology, Univ. Toronto, Banting Inst., 100 College St., Toronto, Ontario M5G 1L5, Canada
Can J Public Health; 72(6):381-385 1981

RADIATION CARCINOGENESIS

4. CELLULAR TRANSFORMATION BY RADIATION: INDUCTION, PROMOTION, AND INHIBITION.

Borek C
Radiological Res. Lab., Cancer Center/Inst. Cancer Res., Columbia Univ. Coll. Physicians and Surgeons, New York, NY, 10032
J Supramol Struct Cell Biochem; 16(4):311-336 1981

5. EFFECTS OF IONIZING RADIATION ON THE DEVELOPING EMBRYO AND FETUS: A REVIEW.

Hoffman DA, Felten RP, Cyr WH
Bureau Radiological Health, Rockville, MD
Effects of Ionizing Radiation on the Developing Embryo and Fetus: A Review. Available from National Technical Information Service, Springfield, VA, as PB82-115379., 160 pp., 1981.

DIETARY FACTORS IN CARCINOGENESIS

6. BETA-CARBOLINES, PSYCHOACTIVE COMPOUNDS IN THE MAMMALIAN BODY.

Airaksinen MM, Kari I
Dept. Pharmacology, Univ. Kuopio, P.O. Box 138, SF-70101 Kuopio 10, Finland
Med Biol; 59(4):190-211 1981

7. DIET AND CANCER OF THE LARGE BOWEL.

Zaridze DG
Analytical Epidemiology Programme, Div. Epidemiology and Biostatistics, International Agency for Res. on Cancer, 150 Cours Albert Thomas, 69372 Lyon, Cedex 2, France
Nutr Cancer; 2(4):241-249 1981

8. INFLUENCE OF DIET ON MAMMARY CANCER.

Carroll KK
Dept. Biochemistry, Univ. Western Ontario, London, Ontario, N6A 5C1, Canada
Nutr Cancer; 2(4):232-236 1981

9. ARTIFICIAL SWEETENERS IN RELATION TO THE EPIDEMIOLOGY OF BLADDER CANCER.

Howe GR, Burch JD
NCI Canada Epidemiology Unit, Univ. Toronto, Ontario, Canada
Nutr Cancer; 2(4):213-216 1981

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

10. EPIDEMIOLOGY AND THE STUDY OF CANCER.

Woods NF, Woods JS
Dept. Physiological Nursing, Sch. Nursing, Univ. Washington, Seattle, WA
Cancer Nursing. Marino LB, ed. St. Louis, The C. V. Mosby Company, 635 pp., 1981.

11. EPIDEMIOLOGY OF CUTANEOUS MALIGNANT MELANOMA.

Balda BR
Dermatologische Klinik und Poliklinik der Universitat, Frauenlobstr. 9-11, D-8000 Munchen 2, W. Germany
MMW; 123(50):1923-1926 1981
In GER

12. THE SMOKING-INDUCED EPIDEMIC.

Doll R
Green Coll. Oxford, Oxford, England
Can J Public Health; 72(6):372-381 1981

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN CARCINOGENESIS

13. HEALTH HAZARDS OF ASBESTOS EXPOSURE.

Kaw JL
Industrial Toxicology Res. Centre, Lucknow 226 001, India
J Sci Ind Res; 40(5):342-346 1981

14. OVERVIEW OF FINNISH EPIDEMIOLOGIC STUDIES ON OCCUPATIONAL CANCER.

Tola S
Dept. Epidemiology and Biometry, Inst. Occupational Health, Haartmaninkatu 1, SF-00290 Helsinki 29, Finland
Scand J Work Environ Health; 7(Suppl4):133-139 1981

CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

15. ALKYLATION OF DNA AND TISSUE SPECIFICITY IN NITROSAMINE CARCINOGENESIS.

Montesano R
International Agency for Res. on Cancer, 150, Cours Albert Thomas, 69372 Lyon Cedex 2, France
J Supramol Struct Cell Biochem; 17(3):259-273 1981

VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

16. TRANSFORMATION INDUCED BY HERPES SIMPLEX VIRUS: A POTENTIALLY NOVEL TYPE OF VIRUS-CELL INTERACTION.

Hampar B
Lab. Molecular Virology, NCI, Frederick, MD, 21701
Adv Cancer Res; 35:27-47 1981

17. ONCOGENESIS BY RNA TUMOR VIRUSES.

Koyama T
Dept. Carcinostasis Res., Tokyo Univ. Medical Res. Inst., 4-6-1 Kindai, Minato-ku, Tokyo 108, Japan
Tanpakushitsu Kakusan Koso; 26(14):2121-2129 1981
In JPN

18. POLYOMA T ANTIGENS.

Eckhart W
Tumor Virology Lab., Salk Inst., San Diego, CA, 92138
Adv Cancer Res; 35:1-25 1981

METHODOLOGY IN CARCINOGENESIS RESEARCH

19. EPIDEMIOLOGICAL ASSESSMENT OF DIETARY INTAKE.

James WP, Bingham SA, Cole TJ
Medical Res. Council's Dunn Clinical Nutrition Center, Adenbrooke's Hosp., Cambridge, England
Nutr Cancer; 2(4):203-212 1981

20. ASSESSMENT OF TECHNOLOGIES FOR DETERMINING CANCER RISKS FROM THE ENVIRONMENT.

Office of Technology Assessment
Office of Technology Assessment, Washington, DC
Assessment of Technologies for Determining Cancer Risks from the Environment. Available from National Technical Information Service, Springfield, VA, as PB81-235400., 243 pp., 1981.

21. ANTIBODIES SPECIFIC FOR DNA COMPONENTS STRUCTURALLY MODIFIED BY CHEMICAL CARCINOGENS.

Muller R, Rajewsky MF
(c/o Rajewsky) Institut fur Zellbiologie (Tumorforschung), Universitat Essen (GH), Hufelandstrasse 55, Essen 1, W. Germany
J Cancer Res Clin Oncol; 102(2):99-113 1981

22. APPLICATION OF THE MICROBIAL MUTATION TEST IN OCCUPATIONAL HEALTH AND ITS FUTURE PROBLEMS.

Takemura N
Dept. Public Health, Jikei Univ., 25-8, Nishi-Shimbashi 2-chome, Minato-ku, Tokyo, 105, Japan
Sangyo Igaku; 23(4):355-365 1981
In JPN

OTHER REVIEWS IN CARCINOGENESIS

23. ARACHIDONIC ACID TRANSFORMATION AND TUMOR PRODUCTION.

Levine L
Dept. Biochemistry, Brandeis Univ., Waltham, MA, 02254
Adv Cancer Res; 35:49-79 1981

24. POLYAMINES IN MAMMALIAN TUMORS PART I.

Scalabrino G, Ferioli ME
Inst. General Pathology, Univ. Milan, 20133 Milan, Italy
Adv Cancer Res; 35:151-268 1981

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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HE 20. 3173/2:

PREVALENCE OF GI CANCER IN HUMAN POPULATIONS

1. A COHORT ANALYSIS OF U.S. STOMACH CANCER MORTALITY 1950-1977.

Manton KG, Stallard E
Center for Demographic Studies, Duke Univ., Box 4732, Duke Station, Durham, NC, 27706
Int J Epidemiol; 11(1):49-61 1982

Models of human carcinogenesis, such as the multi-stage model of Armitage and Doll, are designed to explain the age increase in the incidence of cancers in individuals. As a consequence, a nalyses of population level age-specific death rates via such models are appropriately applied to cohort data where such data are available. In this study a multi-stage model is applied to cohort data for stomach cancer death rates in the United States population for nine distinct cohorts observed over a recent 28-yr period (1950-1977). The multi-stage model parameters obtained from analyses of cross-sectional mortality data under the assumption of no cohort differences in age-specific stomach cancer death rates. (Author abstract) (14 Refs)

2. CANCER MORTALITY IN BARCELONA 1960-1978.

Bosch FX, Orta J, Garcia A, Juvanet J, Camprodon A, Pumarola A
Oncology Service, Hosp. de Sant Pau, Avda S Antonio M Claret, 167, Barcelona 25, Spain
Int J Epidemiol; 11(1):46-48 1982

Cancer mortality rates specific for sex and site for the 1960-1978 period are presented. The population covered is the municipal area of Barcelona. Rates have been adjusted taking as the standard population the Spanish census of 1970. Leading sites for males are lung, stomach and large intestine. Breast, large intestine and stomach are leading causes of death for females. Secular trends follow the general picture of the western industrial countries. (Author abstract) (3 Refs)

3. EPIDEMIOLOGICAL PROSPECTS OF CANCER OF THE LARGE INTESTINE.

Tajima K, Tominaga S
Dept. Epidemiology, Aichi Prefectural Cancer Center, Aichi, Japan
Kango Gijutsu; 27(15):6-11 1981

Although all countries show cancer mortality rates of about 20%, differences in rates are observed which depend on site and dietary habits. Gastric cancer mortality rates are high for both Japanese men and Japanese women, but while mortality rates associated with gastric, uterine, and hepatic cancer are markedly decreasing in the women, those associated with hepatic and lung cancer are increasing in the men. Mortality rates for colon and rectal cancer also have increased markedly in the Japanese. Analysis of international statistics indicates that, for either men or women, mortality rates associated with gastric cancer are inversely related to those associated with cancer of the colon; furthermore, slight increases in mortality rates associated with colon cancer were correlated with large decreases in mortality rates associated with rectal cancer. In Japan, all age groups show increases in mortality rates associated with colon cancer, whereas only the greater than 70-yr-old groups show increases in mortality rates associated with rectal cancer. From 1962-1978, the greatest increases in rates of mortality associated with colon cancer have been observed for cancer of the sigmoid flexure. Further study of the effects of changes in Japanese dietary patterns on the decreasing mortality rates associated with gastric cancer and on the increasing mortality rates associated with colon cancer was thought to be necessary. (12 Refs) (In JPN)

4. CANCER EPIDEMIOLOGY IN CHINA: TWO YEARS OF PROGRESS.

Miller RW
Clinical Epidemiology Branch, NCI, Bethesda, MD
Cancer Research in the People's Republic of China and the United States of America: Epidemiology, Causation and New Approaches to Therapy, Proceedings of a Conference held in New York, 28-29, March, 1980. Marks PA, ed. New York, Grune and Stratton, 273 pp., 1981.

Maps of cancer (CA) mortality in China, ethnic comparison, the Shanghai tumor registry, and CA in domestic animals in China are reviewed. The greatest advance has been in making maps of CA mortality by county. A study revealed that approx 700,000 deaths/yr were due to CA. Ethnic comparison showed that Kazak people have very high rates of CA mortality in general, in particular for esophageal CA. The Uighurs, who live close to the Kazaks, have low rates of CA mortality. The Shanghai tumor registry covers the entire city; data show that CA of the prostate and Ewing's sarcoma of bone are rare, whereas stomach CA is the most frequent form of neoplasia. Gullet CA in chickens and nasal and nasopharyngeal CA in pigs have been studied. (9 Refs)

5. EPIDEMIOLOGY OF GASTRIC CARCINOMA AND GASTRIC REPLACEMENT IN U.S.A..

Longmire WP
Dept. of Surgery, Univ. California Sch. Medicine, Los Angeles, CA, 90024
Med Welt; 33(7):248-253 1982

Epidemiological data show a considerable decrease in the incidence of gastric carcinoma in United States (US) during the past 50 yr, which is probably the result of reduced dietary nitrate exposure. Roux-en-Y esophagojejunostomy is the method used most commonly in US to reconstruct passage following gastrectomy for gastric cancer. (21 Refs) (In GER)

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN GI CARCINOGENESIS

6. OCCUPATIONAL CANCER.

Walker B
Michigan Dept. Public Health, P.O. Box 30035, 3500 N. Logan, Lansing, MI, 48909
J Environ Health; 44(4):176-179 1982

Occupational cancer issues are discussed including the incidence of work-related cancer, local and regional variations, effects of age, socioeconomic considerations, and risk assessment. Vigorous debate exists over the true proportion of cancers of occupational origin due to incomplete reporting systems and heterogeneity of occupational exposures. Viewing occupational cancers as a series of independent problems will focus attention on specific carcinogenic exposures. Local and regional variations are difficult to establish due to differences in terminology and in diagnostic and treatment services. Some trends, such as a higher incidence of lung and colon cancer in the Northeast and in urban areas of the Midwest, do exist. A latency period of 15-40 yr after exposure to environmental agents complicates the study of possibl e primary cancer determinants. The relationship of occupation to various socioeconomic factors makes it difficult to separate the effects on health of each of these factors. It is estimated that billions of dollars are spent on cancer treatment and lost earnings each yr. Recent emphasis on risk assessment has been qualitative identification of carcinogens and risk assessment of the dose-response relationship. Determination of the dividing line between 'significant' and 'insignificant' risk is especially difficult. Risk reduction should include cost benefit analysis. Possibilities for an absolute reduction in the risk of cancer are greater due to increased knowledge of scientific, societal, and technical factos. (12 Refs)

7. CANCER MORTALITY IN A PIGMENT PLANT UTILIZING LEAD AND ZINC CHROMATES.

Sheffet A, Thind I, Miller AM, Louria DB
Dept. Preventive Medicine and Community Health, Univ. Medicine Dentistry New Jersey - New Jersey Medical Sch., 100 Bergen St., Newark, NJ, 07103
Arch Environ Health; 37(1):44-52 1982

Several studies of workers exposed to various forms of chromium compounds have suggested an increased incidence of respiratory cancers. Lead and zinc chromates were among the chromium compounds implicated. The Department of Preventive Medicine and Community Health of the New Jersey Medical School undertook a detailed mortality study of a pigment plant in Newark which utilized both of these compounds. We compared observed deaths from each cause among 1,296 white and 650 non-white males who were employed at the plant between January 1, 1940 and December 31, 1969, with expected deaths, as computed from cause-, age-, and time-specific standard death rates for the United States. A statistically significant relative risk of 1.6 for lung cancer among white male employees was found, as well as among the cohorts of white males employed 10 yr or more. A relative risk of 1.9 was noted for individuals employed at least 2 yr who were at lest moderately exposed to chromates. An increased incidence of lung cancer among non-white males and stomach and pancreatic cancer among the total cohort was also evident. These data support the validity of the association between chromate pigment exposure and lung cancer, suggesting that pigment workers and others exposed to chromate be observed carefully in regard to possible risk of pancreatic and stomach cancers. (Author abstract) (24 Refs)

DIETARY AND DIGESTIVE FACTORS IN GI CARCINOGENESIS

8. DIETARY FIBER.

Kay RM
Dept. Surgery, Toronto Western Hosp., Univ. Toronto, Toronto M5T 2S8, Canada
J Lipid Res; 23(2):221-242 1982

Dietary fiber is plant-derived material that is resistant to digestion by human alimentary enzymes. Fiber may be divided into two broad chemical classes: (1) non-alpha-glucan polysaccharides (cellulose, hemicelluloses, and pectins) and (2) lignins. Dietary fiber behaves within the gastrointestinal tract as a polymer matrix with variable physicochemical properties including susceptibility to bacterial fermentation, water-holding capacity, cation-exchange, and adsorptive functions. These properties determine physiological actions of fiber and are dependent on the physical and chemical composition of the fiber. Fiber undergoes compositional changes as a consequence of bacterial enzymatic action in the colon. Dietary fiber is of clinical significance in certain disorders of colonic function and in glucose and lipid metabolism. Dietary fiber increases stool bulk by acting as a vehicle for fecal water and by increasing fecal bacterial volume. Use of fiber in the treatment of constipation and uncomplicated diverticular disease is well established. By increasing stool bulk, fiber also reduces the fecal concentration of bile acids and other substances. Certain types of fiber decrease the rate of glucose absorption and attenuate postprandial rises in blood glucose and insulin. Plasma cholesterol levels are reduced by mucilaginous forms of fiber. This effect appears to be mediated in part by an increase in fecal acidic sterol excretion. (Author abstract) (266 Refs)

9. CANCER OF THE OESOPHAGUS AND THE USE OF TOBACCO AND ALCOHOLIC BEVERAGES IN TRANSKEI, 1975-6.

McGlashan ND, Bradshaw E, Harington JS
(c/o Harington) Natl. Cancer Assoc. South Africa, P.O. Box 2000, Johannesburg 2000, South Africa
Int J Cancer; 29(3):249-256 1982

A large questionnaire-based sample survey over a period of 2 yr has collected information on tobacco and alcohol use among young and old, male and female respondents in three regions of Transkei selected on the basis of having proved contrasts of incidence experience from esophageal cancer. Results show significant gradients of social fabric and of customary usage of tobacco and alcohol across the three incidence regions. In particular the concept is supported of a synergistic relationship between tobacco and alcohol when both are used by one individual, with the major role being played by tobacco, especially when smoked in pipes. Stress is also laid on contrasts between old and young on the assumption that dynamic shifts of mortality may be expected to follow as the young of today alter the patterns of intake established by their elders. (Author abstract) (10 Refs)

10. FECAL MUTAGENS IN TWO JAPANESE POPULATIONS WITH DIFFERENT COLON CANCER RISKS.

Mower HF, Ichinotsubo D, Wang LW, Mandel M, Stemmermann G, Nomura A, Heilbrun L, Kamiyama S, Shimada A
Dept. Biochemistry and Biophysics, John A. Burns Sch. Medicine, Univ. Hawaii at Manoa, Honolulu, HI, 96822
Cancer Res; 42(3):1164-1169 1982

Human feces from 223 Japanese in Hawaii at high risk for colon cancer and feces from 166 Japanese of northern rural Japan at low risk for colon cancer were shown to contain mutagenic activity under five different test conditions. The first assay, using the Ames TA98 and TA100 Salmonella test, detected ether-soluble mutagens in the presence and absence of rat liver microsomes. Of these, the TA98 direct-acting mutagens are present more frequently in the feces of the high-risk population than the low-risk population at a high level of statistical significance (p less than 0.01). TA98 mutagens activated by rat liver microsomes also occur significantly more frequently in the feces of the Japanese from Hawaii (p less than 0.05). Mutagens detected by TA100 in the presence and absence of rat liver microsomes are not commonly found in either Japanese population. The second bacterial test system used to detect fecal mutagens uses Escherichia coli rec-. This system detects water-soluble fecal mutagens which are also present more frequently in the high-risk population than in the low-risk population (p less than 0.05). (Author abstract) (27 Refs)

11. COFFEE, TEA AND CANCER: HOW TO TEST HYPOTHESES ON LIFESTYLE AND DISEASE?.

Olsson H, Brandt L
Onkologiska kliniken, Lund, Sweden
Lakartidningen; 79(4):196-197 1982

Coffee and tea consumption of 550 tumor patients was analyzed based on questionnaire data. The patients included 19 with seminomas, 36 with cancer of the upper part of the digestive tract (lips, oral cavity, epipharynx, hypopharynx and esophagus), 59 with Hodgkin's disease, 64 with tumors of the larynx and lungs, 36 with thyroid tumors, 120 with cancer of the urinary bladder or kidneys, 28 with skin cancer, 94 with breast cancer, 16 with testicular teratomas, 28 with melanomas, 20 with cancer of the lower parts of the digestive tract (stomach, bile ducts, pancreas, colon and rectum), and 18 with tumors of the paranasal sinuses, auditory meatus and parotid glands. The median coffee consumption of the patients was 3-5 cups/day, ie, approx the same as in the general population. Fifty-three per cent of the patients with seminomas, 50% of those with cancer of the upper part of the digestive tract and 47% of those with Hodgkin's disease consumed large amounts of coffee (5 cups/day or more). The median tea consumption of the patients was 0 cup/day. Forty-four per cent of the patients with testicular teratomas, 31% of those with thyroid tumors, 32% of those with seminomas, and 29% of those with Hodgkin's disease consumed large amounts of tea (2 cups/day or more). The findings indicate that hypotheses based on complex data on lifestyle (education, occupational status, living conditions, dietary and smoking habits, and alcohol consumption) should be tested in epidemiological studies, rather than the possible relationship between tea and coffee consumption, on one hand, and certain diseases, on the other hand. (6 Refs) (In SWE)

12. BILE ACIDS AND CARCINOMA OF THE LARGE BOWEL.

Raedsch R
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Inn Med; 9(1):8-15 1982

Possible correlations between high-fat diets, increased concentration of bile acids in the intestines, and the development of cancer of the colon are discussed. The following aspects of these correlations are considered: metabolism of bile acids, animal models for a relationship between bile acids and colon cancer, bile acids and intestinal bacteria, carcinogenic, cocarcinogenic, and procarcinogenic activities of bile acids, clinical significance of bile acids, and relationship between bile acids and dietary fiber. (74 Refs) (In GER)

13. FLUORIDATION AND CANCER: AN EPIDEMIOLOGIC APPRAISAL.

Neuberger JS
Dept. Community Health, Univ. Kansas Sch. Medicine-Kansas City, Kansas City, KS
J Kans Med Soc; 83(3):134-139 1982

The relationship of water fluoridation to cancer has been studied extensively, perhaps more intensively than many other chemicals in the environment. In 1977, a paper was published under the auspices of the National Health Foundation (NHF), showing a greater increase in the cancer death rates (1940-1970) in the 10 largest American cities that began fluoridation before 1960, as compared to the 10 largest cities not fluoridated as of 1969 (excluding New York City and Detroit). The studies done by the NHF have provided the anti-fluoridationists' greatest arguments against water fluoridation. However, these studies did not meet even minimally acceptable standards for generally accepted epidemiologic research. Other studies by other scientific investigators (including several by the National Cancer Institute) indicate that fluoride is not even associated with cancer, still less a causative factor. The age-adjusted mortality rates in white Kansas residents (both sexes) for 1973-1977 were studied for cancer sites that might possibly be related to water borne carcinogens (stomach, colon, rectum, liver, pancreas, kidney, bladder, and bone), in fluoridated and non-fluoridated Kansas counties of the highest populations. (Wichita, the largest city in Kansas, is not fluoridated). The data were analyzed in terms of person-yr of exposure to fluoride. No association of artificial water fluoridation with cancer was found. It is concluded that current evidence does not support the contention that fluoride is associated with cancer. (9 Refs)

14. STUDIES ON POTENTIAL CARCINOGENS IN THE DIET OF INDIVIDUALS AT HIGH RISK FOR ESOPHAGEAL CANCER.

Li MH
Inst. Cancer Res., Chinese Acad. Medical Sciences, Beijing, People's Republic of China
Cancer Research in the People's Republic of China and the United States of Ameri ca: Epidemiology, Causation and New Approaches to Therapy, Proceedings of a Conference held in New York, 28-29, March, 1980. Marks PA, ed. New York, Grune and Stratton, 273 pp., 1981.

Studies on etiological agents of esophageal cancer in the high-risk areas are discussed. Environmental factors apparently play an important role in the development of esophageal cancer. Some foodstuffs in Linxian are frequently contaminated by Fusarium moniliforme and other fungi. Formation of dimethylnitrosamine, diethylnitrosamine, methylbenzylnitrosamine, and a new volatile N-nitroso compound, N-1-methylacetonyl-N-3-methylbutylnitrosamine has been demonstrated in moldy cornbread after an 8-day incubation, when a small amount of NaNO2 was added initially. Other contributing factors in the environment are nutritional deficiencies in animal protein and fat, vitamins A, B2, and C, high levels of nitrates and nitrites in water and food, low molybdenum and zinc, imbalance of trace elements, and indoor air pollution from coal stoves during the winter. (10 Refs)

OTHER ETIOLOGIC FACTORS IN GI CARCINOGENESIS

15. AN INVESTIGATION OF THE RELATIONSHIP BETWEEN STOMACH CANCER AND CEREBROVASCULAR DISEASE. EVIDENCE FOR AND AGAINST THE SALT HYPOTHESIS.

Whelton PK, Goldblatt P
Div. Nephrology, Johns Hopkins Hosp., 600 North Wolfe St., Baltimore, MD, 21205
Am J Epidemiol; 115(3):418-427 1982

Analysis of age-adjusted death rates in 21 countries during a 20-yr period identified the presence of a strong positive association between recorded mortality from cerebrovascular disease, hypertension and stomach cancer. A study of multiple causes of death was undertaken to determine whether this association results from a unique relationship between these diseases or merely represents a secondary and fortuitous finding. The observed and expected concordances of stomach cancer, lung cancer, pancreatic cancer and cerebrovascular disease with several cardiovascular and non-cardiovascular diagnoses were calculated from tables of multiple causes of death for all persons who died in England and Wales during 1975 and 1976. Although several previously known disease associations were recognized, there was no evidence of a greater concordance between stomach cancer and hypertension or cerebrovascular disease than between lung cancer and hypertension or cerebrovascular disease. Likewise, with one exception, there was no evidence of a greater concordance between stomach cancer and hypertension or cerebrovascular disease than between pancreatic cancer and hypertension or cerebrovascular disease. These results suggest that the temporal and geographic relationships between mortality from cerebrovascular disease, hypertension and stomach cancer are not causally linked. Our findings fail to support the hypothesis that exposure to salt increases an individual's risk of both cerebrovascular disease and stomach cancer. (Author abstract) (20 Refs)

16. CHOLECYSTECTOMY AND THE INCIDENCE OF CANCER OF THE LARGE BOWEL.

Weiss NS, Daling JR, Chow WH
Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA, 98104
Cancer; 49(8):1713-1715 1982

As part of an epidemiologic study of cancer of the large bowel in women, female residents of King and Pierce counties (Washington) who were diagnosed during 1976-77 were interviewed regarding previous gallbladder surgery. Their responses were compared with those of a random sample of women from the same population. A history of cholecystectomy was somewhat more frequent among patients with colon cancer than among controls - we estimate the colon cancer risk in women without a gallbladder to be 1.4x that of other women - but the 95% confidence limits of the relative risk included 1.0 (0.8-2.5). There was no association between cholecystectomy and rectal cancer and, among the subsites of colon cancer, the magnitude of the excess risk failed to show any consistent right-left gradient. Nonepidemiologic data suggest that cholecystectomy could increase the risk of colon cancer. However, if such an association truly exists it is not a strong one, and studies larger than those conducted to date are needed to detect this association reliably. (Author abstract) (15 Refs)

17. LACK OF ASSOCIATION OF CYTOMEGALOVIRUS WITH ADENOCARCINOMA OF THE COLON.

Hart H, Neill WA, Norval M
(c/o Norval) Dept. Bacteriology, Univ. Edinburgh Medical Sch., Teviot Place, Edinburgh EH8 9AG, Scotland
Gut; 23(1):21-30 1982

Tumor specimens from patients with adenocarcinoma of the colon or rectum were examined for the presence of cytomegalovirus (CMV), and specimens of normal mucosa from the same patients were studied in parallel. Frozen sections of 14 specimens were made and the presence of CMV mRNA assayed by in situ hybridization using 3H-labeled CMV-DNA as a probe. Nine of these sections were also tested for cytomegalovirus antigens by immunofluorescence. No viral nucleic acids or antigens were detected. In addition to these direct approaches, the specimens were disaggregated and 19 were successfully cultured in various media over several months without yielding virus on any occasion. Areas containing epithelial cells were found in some cultures, foci of bipolar cells in others, while, in several, fibroblastic cells predominated. To ensure that any virus-containing cells were not lost by this method, the disaggregated tumor and normal intestinal cells were directly co-cultivated and also fused with human embryo lung cells, which are permissive for cytomegalovirus replication. The resulting cultures were examined over 2 to 3 mo for the presence of cytomegalovirus, and in no instance was virus found, despite attempted induction by iododeoxyuridine. Two fusion cultures became contaminated with cytomegalovirus, strain AD-169, which was being handled in the laboratory at the same time. The strain was identified by the pattern of viral DNA fragments produced by restriction endonuclease cleavage. Thus the accidental passage of virus in the heterokaryons did not alter its DNA and would further indicate the absence of any cytomegalovirus genomes in the adenocarcinoma cells. (Author abstract) (34 Refs)

18. THE RISK OF SECOND PRIMARIES SUBSEQUENT TO IRRADIATION FOR CERVIX CANCER.

Lee JY, Perez CA, Ettinger N, Fineberg BB
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Int J Radiat Oncol Biol Phys; 8(2):207-211 1982

The risk of developing a new primary malignancy following radiation therapy (RT), alone or combined with surgery, for invasive cancer of the uterine cervix was studied in 1,048 patients with histologically proven invasive carcinoma Stages I, II, or III, who were followed up with a median period of 4 yr. During the observation time 32 second primaries (SP) were reported. No statistically significant difference between the observed and expected number of SP was noted. Using the person yr approach, the SP incidence rate was 5.49/1,000 person-yr. Eleven SP were observed in the pelvic region: colon, rectum, endometrium, and vagina, while 20 occurred outside the pelvis. Neither the incidence of pelvic SP nor that of extra-pelvic SP was greater than expected. The time from RT to diagnosis of a SP ranged from 1 to 16 yr with a median of 8 yr for pelvic SP, and 6 yr for extra-pelvic SP. The incidence of SP increased with the stage of cervix cancer; the increase is statistically significant. Mean ages of Stage II and Stage III patients were higher than that of Stage I patients. No significant difference of a possible carcinogenic effect of RT was noted between the patients treated with RT alone (6,000-8,000 rad) and patients treated preoperatively or postoperatively (3,000-5,000 rad). SP had no impact on the survival experience of the study population in the first 5 yr after treatment; after 5 yr some deaths were observed, but patients are at higher risk of death from other causes than from SP. (15 Refs)

19. CORRELATES OF HOMOSEXUAL BEHAVIOR AND THE INCIDENCE OF ANAL CANCER.

Daling JR, Weiss NS, Klopfenstein LL, Cochran LE, Chow WH, Daifuku R
Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA, 98104
JAMA; 247(14):1988-1990 1982

To determine whether characteristics that are correlated with male homosexual behavior are associated with the incidence of cancer, the names of persons with a diagnosis of cancer in western Washington during 1974 to 1979 were linked to those in the state syphilis registry. Eight of 47 men with anal cancer were found to have had a reactive FTA test result; the expected number, based on the proportion of reactive cases among men with other sites of cancer, was only 0.40. Among men with anal cancer identified through 10 population-based cancer-reporting systems in the United States, 24.4% had never been married, compared with 7.8% of men with colon and rectal cancer. Neither of these relationships was observed for women with anal cancer. Because in men, but not in women, having had syphilis and being single are associated with the practice of anal intercourse, our data suggest that anal intercourse may be a risk factor for anal cancer. (Author abstract) (19 Refs)

20. SURVIVAL WITH CARCINOMA ARISING IN MUCOSAL ULCERATIVE COLITIS.

Lavery IC, Chiulli RA, Jagelman DG, Fazio VW, Weakley FL
Dept. Colon and Rectal Surgery, Cleveland Clinic, 9500 Euclid Ave., Cleveland, OH, 44106
Ann Surg; 195(4):508-512 1982

Adenocarcinoma of the colon is a well-recognized complication of total chronic ulcerative colitis. The incidence increases with time, and the carcinoma arising in chronic ulcerative colitis has developed a bad clinical reputation in terms of aggressive behavior. The survival statistics of patients with cancer arising in chronic ulcerative colitis are compared with statistics for a group of noncolitic patients with equivalent clinicopathologic staging treated at the same institution. When grouped by extended Duke's classification and compared with carcinoma arising without ulcerative colitis, there was no statistical difference in survival rates. The overall results are worse because of the higher percentage of patients with incurable disease at the time of operation. With improved surveillance and methods of detecting premalignant changes, the necessity for prophylactic proctocolectomy should decline. (Author abstract) (28 Refs)

21. CHRONIC INFLAMMATORY DISEASES OF INTESTINES AND RISK OF CANCER.

Costa AC, Bettarello A
Dep. Clin., Fac Medicina da Univ. de Sao Paulo, Sao Paulo, Brazil
Rev Hosp Clin Fac Med Sao Paulo; 36(5):189-193 1981

Chronic inflammatory diseases of the intestine and their relationship to cancer were considered. Especially Crohn's disease and unspecific ulcerative colorectitis were examined. Incidence of cancer in patients with these diseases is higher than in population in general, but only a very small number of patients will develop cancer. Difficulties in diagnosing cancer in such patients were discussed. (36 Refs) (In POR)

22. PRECANCEROUS CONDITIONS AND CANCER OF THE STOMACH.

Duris I, Koska M, Zaviacic M, Mikulecky M, Holly D
Katedra internistickych disciplin, I Lekarska fakulta Univerzity Komenskeho, Mickiewiczoya 13, 88421 Bratislava, Czechoslovakia
Bratisl Lek Listy; 76(5):540-551 1981

Precancerous conditions and cancer of the stomach were studied in 4,159 patients subjected to gastroscopy. The histological diagnosis was that of gastric polyps in 112 patients, atrophic gastritis with intestinal metaplasia (AGIM) in 190, and gastric cancer in 103, including intramucosal carcinoma in 9. All patients with gastric carcinomas were in the age bracket 20-90 yr, and the frequency was higher among men than among women in all age groups. The incidence of AGIM was higher among women than among men in the age group 40-70 yr, especially in the age group 50-60 yr. Gastric cancer was found to occur at a significantly higher age among agricultural workers than in the other occupational groups. Concurrent disease as risk factor was found in 47% of 42 patients with gastric xanthomas. Gastric stump carcinoma was found in 23% of the patients subjected to gastric resection for gastric or duodenal ulcer. Forty-two parameters were studied in the gastric cancer patients and in patients without this disease by the pattern recognition method. Consumption of garlic, onions, home made smoked meat, as well as persistent emotion of fear were found to be linked most closely with gastric cancer. Restriction of burnt food and consumption of generous amounts of fruits and vegetables appear to be beneficial against gastric cancer. (41 Refs) (In SLO)

INDUCTION OF GI CARCINOGENESIS IN ANIMALS

23. THE CARCINOGENIC EFFECT OF 1,1-DIETHYL-3-METHYL-3-NITROSOUREA IN EUROPEAN HAMSTERS.

Ketkar MB, Althoff J, Lijinsky W

Abteilung fur experimentelle Pathologie, Medizinishe Hochschule Hannover, Karl-Wiechert-Allee 9, D - 3000 Hannover 61, W. Germany

Exp Pathol; 20(3):153-155 1981

Laboratory-bred European hamsters received subcutaneous injections of 1,1-diethyl-3-methyl-3-nitrosourea once weekly for life. The animals developed mainly squamous cell carcinomas of the nasal and oral cavities and malignant sarcomas (schwannomas) of the glandular stomach. The av tumor latency was shorter in females (24 wk) than in males (28 wk), while tumor incidence was 80% for both sexes. (Author abstract) (10 Refs)

24. CARCINOGENICITIES OF 1-ETHYL- AND 1-AMYL-1-NITROSOURETHANS IN FEMALE DONRYU RATS: DOSE-EFFECT RELATIONS.

Onodera H, Furuta K, Matsuoka C, Kamiya S, Maekawa A

(c/o Maekawa) Div. Pathology, Biological Safety Res. Center, Kamiyooga 1-18-1, Setagaya-ku, Tokyo 158, Japan

Gan; 73(1):48-54 1982

Groups of female Donryu rats were given solutions of 100, 50, and 25 ppm of 1-ethyl-1-nitrosourethan (ENUR), and of 400, 200, and 100 ppm of 1-amyl-1-nitrosourethan (ANUR) continuously in the drinking water. The incidence of tumors was nearly 100% in all groups treated with ENUR or ANUR, but with both chemicals that rats showed dose-dependent mean survival times. In the groups treated with ENUR, tumors were most frequent in the upper digestive tract and duodenum, whereas in groups given ANUR tumors were induced only in the upper digestive tract, with none in the duodenum. Tumors of the forestomach were more frequent than those of the esophagus and oral cavity and/or pharynx in groups treated with ENUR. In contrast, the target organs of ANUR were the oral cavity and/or pharynx, and the esophagus, rather than the forestomach. The carcinogenicities of these two chemicals are discussed in comparison with those of other 1-alkyl-nitrosourethans. (Author abstract) (16 Refs)

MECHANISMS AND MODIFICATIONS OF GI CARCINOGENESIS

25. EFFECT OF AGING ON THE DEVELOPMENT OF 1,2-DIMETHYLHYDRAZINE-INDUCED INTESTINAL TUMORS IN MICE.

Turusov VS, Lanko NS, Parfenov IuD
Lab. Carcinogenic Agents, All-Union Cancer Res. Center, Moscow, USSR
Biull Eksp Biol Med; 91(12):705-707 1981

Relationship between carcinogenesis and aging was studied in young (2 mo old), mature (8 mo old), and old (12 mo old) female CBA mice. Animals received sc injections of 1,2-dimethylhydrazine (DMH: 8 mg/kg, 1x/wk). Animals were followed up for 26-35 wk after the initiation of DMH administration, and the incidence of tumors of the large intestine was determined. An overall incidence of tumors in young, mature, and old mice was 13.1%, 61.0%, and 69.1%, respectively. The frequency of infiltrating tumors was 6%, 30.5%, nad 54.3%, respectively. Analysis of time-effect curves showed that the median latent period of tumor development in young mice was approx 1.8x greater than that in old mice and 1.4x greater than that in mature mice. The differences in the chemical carcinogenesis were explained by elevated activity of beta-glucuronidase in the large intestine of old mice. (7 Refs) (In RUS)

26. ENHANCED EFFECT OF GASTRIN ON RAT STOMACH CARCINOGENESIS INDUCED BY N-METHYL-N'-NITRO-N-NITROSOGUANIDINE.

Tahara E, Shimamoto F, Taniyama K, Ito H, Kosako Y, Sumiyoshi H
Dept. Pathology, Hiroshima Univ. Sch. Medicine, 1-2-3 Kasumi, Minami-ku, Hiroshima 734, Japan
Cancer Res; 42(5):1781-1787 1982

This study deals with the effects of gastrin on the incidence of gastric tumors in rats induced by N-methyl-N'-nitro-N-nitrosoguanidine. Inbred Basel-Wistar rats received N-methyl-N'-nitro-N-nitrosoguanidine in drinking water (50 ug/ml for 32 wk) in order to produce gastric carcinoids. A treatment with sc injection of pentagastrin (300 ug/kg, once daily for 4 wk) was started at the beginning of N-methyl-N'-nitro-N-nitrosoguanidine treatment simultaneously, on the 4th, 8th, 16th, and 32nd wk after start of N-methyl-N'-nitro-N-nitrosoguanidine treatment, respectively. At autopsy, from the 55th to 60th wk after start of the experiment, only in the 8th-wk group of gastrin-treated rats was the incidence of gastric carcinoid significantly higher than in the gastrin-untreated group of rats receiving N-methyl-N'-nitro-N-nitrosoguanidine alone. The incidence of adenocarcinoma in t he glandular stomach also was high only in the 4th-wk group of gastrin-treated rats. However, these effects could not be seen in other gastrin-treated or untreated groups of rats. The data suggest that gastrin treatment in the early stage of rat stomach carcinogenesis by N-methyl-N'-nitro-N-nitrosoguanidine is effective in increasing the development of gastric tumors. (Author abstract) (21 Refs)

27. INHIBITION OF METHYLAZOXYMETHANOL-INDUCED INTESTINAL TUMORS IN THE RAT BY PYRAZOLE WITH PARADOXICAL EFFECTS ON SKIN AND KIDNEY.

Notman J, Tan QH, Zedeck MS
(c/o Zedeck), Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Cancer Res; 42(5):1774-1780 1982

Methylazoxymethanol is a potent carcinogen and induces tumors predominantly of the small intestine and colon following a single injection. Previous data indicated that alcohol dehydrogenase could convert this carcinogen to a reactive alkylating agent. Rats were treated with an inhibitor of this enzyme, pyrazole, 2 hr prior to their receiving the carcinogen. The development of intestinal and colonic tumors was prevented. The rats did, however, develop numerous tumors of the skin and kidney. Analyses of the complete autopsies are presented. The data indicate that intestinal and colonic alcohol dehydrogenase plays a role in the tumorigenic effects of methylazoxymethanol and that other non-pyrazole-sensitive enzymes exist in other organs that can also activate this carcinogen. (Author abstract) (21 Refs)

BIOCHEMICAL, MORPHOLOGICAL AND IMMUNOLOGICAL ASPECTS OF GI CARCINOGENESIS

28. METABOLISM OF N-NITROSAMINES BY CULTURED HUMAN AND RAT ESOPHAGUS.

Autrup H, Stoner GD
NCI, NIH, Building 37, Room 2C13, Bethesda, MD, 20205
Cancer Res; 42(4):1307-1311 1982

The metabolism of several N-nitrosamines (N-nitrosodimethylamine, N-nitrosoethylmethylamine, N-nitrosodiethylamine, N-nitrosobenzylmethylamine, and N-nitrosopyrrolidine) in cultured human and rat esophagus has been investigated by measuring CO2, metabolites with an oxo group and metabolites bound to DNA. Both acyclic and cyclic N-nitrosoamines were metabolized by rat esophagus. The highest level of metabolite binding was seen with N-nitrosobenzylmethylamine, an organotropic carcinogen for the rat esophagus. The binding level was about 100-fold higher than in human esophagus. This compound methylated rat esophageal DNA at positions 7 and O6 of guanine. The level of benzylation in rat was one-tenth the level of methylation. Formation of benzaldehyde exceeded that of formaldehyde plus CO2 by a factor of 6, indicating that the methylene group was preferentially oxidized. N-Nitrosoethylmethylamine was preferentially oxidized by rat esophagus in the ethyl group. The highest binding level to DNA from this compound was observed with the methyl group. No binding was detected to human esophagus. N-Nitrosopyrolidine wa s oxidized by both rat and human esophagus in the alpha position, as measured by the formation of 2,4-dinitrophenylhydrazone derivative of 4-hydroxybutanal. Binding of metabolites of N-nitrosopyrrolidine to DNA was detected only in rat esophagus. As measured by the formation of both CO2 and formaldehyde, N-nitrosodimethylamine was metabolized by both human and rat esophagus. While most of the radioactivity associated with DNA was found to be incorporated into guanine and adenine, methylation of the guanine positions 7 and O6 was detected by chromatography of the hydrolyzed rat DNA. The results indicate significant quantitative and perhaps qualitative differences between cultured rat and human esophagus in their ability to activate N-nitrosamines, although unknown physiological differences after culture may contribute to this difference. (44 Refs)

29. BIOCHEMICAL LOCALIZATION OF ARYL HYDROCARBON HYDROXYLASE IN THE INTESTINAL EPITHELIUM OF THE RAT.

Porter CW, Dworaczyk D, Gurtoo HL

Dept. Experimental Therapeutics, Grace Cancer Drug Center, Roswell Park Memorial Inst., New York State Dept. Health, Buffalo, NY, 14263

Cancer Res; 42(4):1283-1285 1982

The distribution of the carcinogen-metabolizing enzyme system, aryl hydrocarbon hydroxylase (AHH), was biochemically determined in the intestinal epithelium of the rat. A method of epithelial cell isolation in which fractions of cells are sequentially collected as a villus tip-to-crypt gradient was used. AHH activity was highest in the midvillus region, 40% lower at the villus tip, and practically nonexistent in the crypt region where active cell proliferation takes place. This distribution differed from those of sucrase and alkaline phosphatase (used here as markers for cellular differentiation), which were characteristically lowest in activity at the crypts and increased continuously to the villus tips. Conceivably, the midvillus peak of AHH activity may serve to protect or enhance the susceptibility of cells undergoing cell division in the nearby crypt regions, depending on whether the predominant function of AHH in the intestinal epithelium involves detoxication or activation of polyaromatic carcinogens. (Author abstract) (16 Refs)

30. MORPHOGENESIS OF COLONIC CARCINOMA. ULTRASTRUCTURAL STUDIES OF AZOXYMETHANE-INDUCED EARLY LESIONS IN COLON EPITHELIUM OF FISCHER 344 RATS.

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Dept. Pathology, Univ. Maryland Sch. Medicine, 10 S Pine St., Baltimore, MD, 21201

Arch Pathol Lab Med; 106(3):140-144 1982

Marked dilation and distortion of the crypts have been observed in the colonic epithelium of Fischer-344 rats after four to six weekly doses of azoxymethane (8 mg/kg). These changes precede malignant transformation in this model and, therefore, may be considered premalignant. Ultrastructural morphologic aspects of these crypts can arbitrarily be divided into three stages: an early stage of increased mucus secretion and 'exhausted' appearance of mucous cells; an intermediate stage of severe crypt dilation, with extreme thinning of crypt epithelium and neutrophilic emigration to the mucous pool of the crypt lumen; and a late stage characterized by repopulation of the crypts, with epithelial cells showing an increased nuclear-cytoplasmic ratio and bizarre nuclei and nucleoli. The surface epithelium between the crypts shows increased cell loss and alterations of cell membrane. Similar structure of crypts has been described in the mucosa remote from carcinoma in rats and humans, and in various precancerous changes in humans (ie, ulcerative colitis and Crohn's disease). Therefore, I propose that these lesions are significant in human colon carcinogenesis as well. (Author abstract) (14 Refs)

31. ARGYROPHIL CELLS IN ADENOMAS OF FAMILIAL POLYPOSIS COLI.

Okayasu I, Hatakeyama S, Iwama T, Utsunomiya J

First Dept. Pathology, Sch. Medicine, Tokyo Medical and Dental Univ., Tokyo, Japan

Bull Tokyo Med Dent Univ; 28(1):1-5 1981

The distribution of argyrophilic (ARG) cells in colonic mucosa was studied in resected ascending and sigmoid colon specimens from 15 patients (20-53 yr old) with familial polyposis coli (FPC: 12/15 patients belonged to 4 families) and uninvolved colonic mucosa from 5 control patients (28-70 yr old) with colonic adenocarcinomas unrelated to FPC. In the normal mucosa from FPC patients and controls and in the FPC adenomas, the frequency of ARG cells was significantly higher in the sigmoid colon than in the ascending colon. Scattered ARG cells were found in some of the FPC adenomas (especially of the sigmoid colon), but at a much lower frequency than in the nontumorous mucosa. ARG cells were found only in adenomas showing slight dysplasia and never in adenomas with moderate or severe dysplasia. Sigmoid adenomas from 6/15 FPC patients contained at least 10 ARG cells/adenoma. Three of the patients belonged to one family (represented by five members of the FPC group), suggesting that a gene related to the appearance of many ARG cells in FPC adenomas may be involved. Foci and ARG cells were observed in some FPC adenomas of the sigmoid colon (never the ascending colon), suggesting that the ARG cells might actively participate in growth of these tumors. (8 Refs)

32. CARCINOID TUMORS OF THE GASTROINTESTINAL TRACT. TUMORAL PATHOLOGY OF THE DIFFUSE ENDOCRINE SYSTEM OF THE GASTROINTESTINAL TRACT.

Wallon J, Rahier J, Noel H, Hoat J

Service d'Anatomie Pathologique, Cliniques Universitaires Saint-Luc, Avenue Hippocrate 10, B-1200 Brussels, Belgium

Rev Fr Gastroenterol; (174):45-51 1981

There are listed eight endocrine cell types which secrete peptides hormones and biogenic amines in the gastrointestinal system. The identification of these cell types is based on ultrastructural bases. Like other cellular systems, the diffuse endocrine system can present several modes of pathological proliferation. One can distinguish simple hyperplasia, micro-invasive tumors (microcarcinoids) and invasive proliferation (carcinoid tumors). Microcarcinoids never invade beyond the muscularis mucosa (MM). The infiltration of the MM constitutes a major criterion in the differential diagnosis between noninvasive and invasive forms. Histochemical analysis provides the basis of a diagnosis when routine macroscopic and microscopic analysis have led to the suspicion of an endocrine tumor. It has not yet been possible to establish a classification for endocrine type tumors based on their peptide secretion because numerous tumors contain several cell types which secrete different hormones even though there is often a predominant secretion type. Also, specific antibodies for all the digestive hormones have not yet been developed and it is not yet possible to characterize the precise manner of secretion of each tumor. (16 Refs) (In FRE)

33. HUMAN COLON TUMOR ANTIGENS.

Yeoman LC, Taylor CW, Chakrabarty S
Nuclear Protein Lab., Dept. Pharmacology, Baylor Coll. Medicine, Houston, TX, 77030
Methods Cancer Res; 19:233-271 1982

Colon cancer marker biology, cellular fractionation and antibody preparation, radioimmunoelectrophoresis, immunolocalization of GW-39 hamster colon tumor antigens, and purification and properties of colon antigens are reviewed. Subcellular fractionation of GW-39 colon adenocarcinoma cells into cytoplasmic and nuclear fractions yielded extracted antigens, which may have been dominated by other molecules when presented to a xenogeneic host as a group. Three potential antigen markers have been detected which share no immunological cross-reactivity with carcinoembryonic antigen. One of these, antigen 3, a glycoprotein of approx 150,000 mol wt, is most highly purified and characterized to date. Cancer marker molecules aid in the investigation of the biological mechanism involved in tumor promotion, carcinogenesis, or maintenance of cancer phenotype. (91 Refs)

34. EFFECT OF BUTYLATED HYDROXYANISOLE, ALPHA-ANGELICA LACTONE, AND BETA-NAPHTHOFLAVONE ON BENZO(A)PYRENE:DNA ADDUCT FORMATION IN VIVO IN THE FORESTOMACH, LUNG, AND LIVER OF MICE.

Ioannou YM, Wilson AG, Anderson MW
(c/o Anderson) Lab. Pharmacology, Natl. Inst. Environmental Health Sciences, NIH, Research Triangle Park, NC, 27709
Cancer Res; 42(4):1199-1204 1982

The effects of alpha-angelica lactone (alpha-AL), butylated hydroxyanisole (BHA), and beta-naphthoflavone (beta-NF) on the amount of benzo(a)pyrene (BP) metabolite:DNA adducts formed in the forestomach, lung, and liver of ICR/Ha mice were investigated 48 hr after po administration of BP. BP was administered to mice in amounts known to result in BP-induced neoplasia in certain tissues. Analysis of deoxyribonucleosides by high-pressure liquid chromatography showed that several BP metabolite:DNA adducts were formed in each tissue examined. The major identified adduct in each tissue cochromatographed with the (+-)-7beta,8alpha-dihydroxy-9alpha,10alpha-epoxy 7,8,9,10-tetrahydrobenzo(a)pyrene (BPDEI):deoxyguanosine adduct. The (+-)-7beta,8alpha-dihydroxy-9beta,10beta-epoxy-7,8,9,10 tetrahydrobenzo(a)pyrene (BPDEII):deoxyguanosine adduct was detected in each of the tissues. As a percentage of total DNA-associated radioactivity, the BPDEI:DNA and BPDEII:DNA adducts accounted for 14% in the forestomach, 39% in the lung, and 3% in the liver. Another adduct, possibly derived from BP: phenol(s), was detected in lung and liver. Early eluting unidentified DNA-associated radioactivity was also present in each of the tissues and accounted for the majority of the radioactivity (88% in forestomach, 57% in lung, and 97% in liver). Although total DNA-associated radioactivity in liver was approximately 15-fold higher than in lung and 5-fold higher than in forestomach, the specific activities of the BPDEI:adducts and of the BPDEII:adducts were approximately the same in these organs. Addition of alpha-AL or BHA to the diet inhibited BPDEI:DNA adduct formation in the forestomach and liver but not in the lung. The effect of beta-NF was not tissue specific; this aryl hydrocarbon hydroxylase inducer decreased markedly (80 to 90%) BPDEI:DNA adduct formation in all three tissues. The radioactivity associated with the early eluting peaks was also reduced when alpha-AL, BHA, or beta-NF was fed to the mice. The inhibition of BPDEI:DNA and BPDEII:DNA adduct formation by alpha-AL, BHA, and beta-NF is discussed in relation to similar studies where these compounds inhibited BP-induced neoplasia. (Author abstract) (53 Refs)

35. ISOLATION AND IDENTIFICATION OF KAHWEOL PALMITATE AND CAFESTOL PALMITATE AS ACTIVE CONSTITUENTS OF GREEN COFFEE BEANS THAT ENHANCE GLUTATHIONE S-TRANSFERASE ACTIVITY IN THE MOUSE.

Lam LK, Sparnins VL, Wattenberg LW
Dept. Lab. Medicine and Pathology, Univ. Minnesota, Minneapolis, MN, 55455
Cancer Res; 42(4):1193-1198 1982

Glutathione S-transferase is a major detoxification enzyme system that catalyzes the binding of a variety of electrophiles, including reactive forms of chemical carcinogens, to glutathione (GSH). Green coffee beans fed in the diet induce increased GSH S-transferase activity in the mucosa of the small intestine and in the liver of mice. A potent compound that induces increased GSH S-transferase activity was isolated from green coffee beans and identified as kahweol palmitate. The corresponding free alcohol, kahweol, and its synthetic monoacetate are also potent inducers of the activity of GSH S-transferase. A similar diterpene ester, cafestol palmitate, isolated from green coffee beans was active but less so than was kahweol palmitate. Likewise, the corresponding alcohol, cafestol, and its monoacetate showed moderate potency as inducers of increased GSH S-transferase activity. Kahweol palmitate and cafestol palmitate were extracted from green coffee beans into petroleum ether. The petroleum ether extract was fractionated by preparative normal-phase and reverse-phase liquid chromatographies successively. Final purification with silver nitrate-impregnated thin-layer chromatography yielded the pure palmitates of cafestol and kahweol. The structures were determined by examination of the spectroscopic data of the esters and their parent alcohols and by derivative comparison. (Author abstract) (22 Refs)

36. COMPARISON OF BENZO(A)PYRENE METABOLISM IN BRONCHUS, ESOPHAGUS, COLON, AND DUODENUM FROM THE SAME INDIVIDUAL.

Autrup H, Grafstrom RC, Brugh M, Lechner JF, Haugen A, Trump BF, Harris CC
LHC, NCI, Building 37/2C13, Bethesda, MD, 20205
Cancer Res; 42(3):934-938 1982

The metabolism of benzo(a)pyrene has been investigated in cultured normal human bronchus, colon, duodenum, and esophagus obtained from the same patient. The highest total metabolism was found in bronchus and duodenum, while the highest mean binding level was observed in the bronchus followed, in order, by the esophagus, duodenum, and transverse colon. A 30-fold interindividual variation in the binding level was found in each of the four organs studied, and a positive correlation between the binding levels in bronchus, colon, and duodenum was found. In human bronchus, a positive correlation was found between level of binding of benzo(a)pyrene to DNA and the amount of both benzo(a)pyrene 7,8-diol and the combined group of 3-hydroxybenzo(a)pyrene, benzo(a)pyrene 9,10-diol, and water-soluble metabolites. A significantly higher relative amount of benzo(a)pyrene tetrols and benzo(a)pyrene 9,10-diol was found by human bronchus compared to the gastrointestinal tissues, while a higher level of benzo(a)pyrene was formed by the latter. The relative distribution of benzo(a)pyrene-DNA adducts was similar in all four organs, the major DNA adduct being formed by trans-addition of anti-7,8-dihydroxy-9,10-epoxide-7,8,9, 10-tetrahydrobenzo(a)pyrene to the 2-amino group at guanine. These results indicate that the metabolism of benzo(a)pyrene by at least four different organs is qualitatively similar but that quantitative differences exist. (Author abstract) (46 Refs)

37. CHARACTERIZATION OF THE CONSTITUENT FATTY ACIDS IN THE PHOSPHOGLYCERIDES OF CHEMICALLY INDUCED POLYCYSTIC DISEASE AND GASTRIC TUMOR IN RAT.

Ryuzaki M, Ohta A, Oshima M

Dept. Biology, Kitasato Univ. Sch. Medicine, Sagamihara, Kanagawa 228, Japan

Dev Growth Differ; 23(5):507-513 1981

The positional distribution of fatty acids in choline phosphoglycerides and other phospholipids in hepatoma and other tumors is different from distribution in corresponding normal tissues; this difference may be due to changes in positional distribution of fatty acids in membrane phospholipids. One year old BN rats of both sexes received tap water containing 0.009% N-methyl-N'-nitro-N-nitrosoguanidine to induce polycystic disease or gastric tumors. After 10 mo, whole livers and whole stomachs of experimental and control rats were analyzed for phospholipid classes. In diseased rats, choline phosphoglyceride was about one half that of normals; sphingomyelin content was increased in diseased livers. With regard to composition of fatty acids at the 1-position, diseased livers showed an increase of approx 22% in 16:0 fatty acid and a decrease of approx 12% in 18:1 fatty acid. In diseased organs, fatty acids at the 2-position showed greater saturation. An increase in 15:0 fatty acid at the 2-position of ethanolamine phosphoglycerides was observed in diseased organs. (18 Refs)

PANCREATIC CARCINOGENESIS

38. IDENTIFICATION OF 7-CARBOXYMETHYLGUANINE IN DNA FROM PANCREATIC ACINAR CELLS EXPOSED TO AZASERINE.

Zurlo J, Curphey TJ, Hiley R, Longnecker DS

(c/o Longnecker) Dept. Pathology, Dartmouth Medical Sch., Hanover, NH, 03755

Cancer Res; 42(4):1286-1288 1982

Studies were undertaken to determine the identity of an azaserine:DNA adduct. The most probable adduct, 7-carboxymethylguanine, was synthesized. DNA isolated from pancreatic acinar cells treated in culture with [14C]azaserine was hydrolyzed under neutral conditions to liberate N-alkylated purines. The neutral hydrolysate was subjected to high-performance liquid chromatography along with the synthetic standard. One of the radioactive peaks from the treated DNA was found to cochromatograph with 7-carboxymethylguanine in three systems: reverse phase; anion exchange; and ion pair reverse phase. These results suggest that azaserine metabolism in acinar cells results in carboxymethylation of DNA, supporting previously proposed models of azaserine degradation. (Author abstract) (20 Refs)

39. THE PERSISTENCE OF DNA DAMAGE IN THE PANCREAS OF SYRIAN GOLDEN HAMSTERS TREATED WITH N-NITROSOBIS(2-OXOPROPYL)AMINE.

Lawson T, Hines L, Helgeson S, Pour P

Eppley Inst. for Res. in Cancer, Univ. Nebraska Medical Center, 4315 Dewey Ave., Omaha, NE, 68105

Chem Biol Interact; 38(3):317-323 1982

DNA damage was estimated in the liver, pancreas and salivary gland of Syrian hamsters given N-nitrosobis(2-oxopropyl)amine (BOP) by alkaline sucrose gradient centrifugation. A single BOP dose (10 mg/kg) produced in all three tissues extensive DNA damage that was largely repaired in the salivary gland by 4 wk, while in the liver and pancreas, some DNA damage persisted until 4 wk. When higher BOP doses (20 and 40 mg/kg) were used, considerable DNA damage was still evident in the pancreas, but not in the liver at 6 wk. Greater damage persisted in hamsters given 40 mg/kg, compared with those administered 20 mg/kg. (Author abstract) (8 Refs)

40. EPIDEMIOLOGIC STUDY OF REFINERY AND CHEMICAL PLANT WORKERS.

Hanis NM, Holmes TM, Shallenberger LG, Jones KE

Exxon Corporation, P.O. Box 235, E. Millstone, NJ, 08873

JOM; 24(3):203-212 1982

A dynamic retrospective cohort study was performed to examine the mortality experience of workers at Exxon's Baton Rouge, La, refinery and chemical plant. Included were 8,666 regular employees who worked at least 1 mo during the period January 1, 1970 through Dec 31, 1977, and retirees who were alive as of Jan 1, 1970. Mortality from all causes of death was lower than expected when compared with that of the U S population of similar age, sex, and race. Analyses of mortality by specific site of cancer revealed elevated standardized mortality ratios (SMRs) for cancer of the kidney, testis, brain/central nervous system, pancreas, and lymphopoietic sites; none of these elevations was statistically significant. Because of the higher than av mortality from cancer of the pancreas in some Louisiana parishes and the observation that one additional death from cancer of the pancreas in this study would have resulted in a statistically significant SMR at the 95% confidence level, some emphasis was placed on this finding. No evidence was found to link cancer of the pancreas to a specific occupational group. An examination of mortality by occupational class revealed some elevated SMRs for further study. (Author abstract) (24 Refs)

41. COMPARATIVE STUDIES OF NEOPLASTIC RESPONSE TO A SINGLE DOSE OF NITROSO COMPOUNDS. 7. THE EFFECT OF N-NITROSOBIS (2-HYDROXYPROPYL)AMINE IN SYRIAN GOLDEN HAMSTERS.

Pour PM, Salmasi SZ

Preclinical Res., Toxicology Dept., Sandoz AG, CH-4133 Pratteln 4, Switzerland

J Cancer Res Clin Oncol; 102(3):265-269 1982

Single sc applications of N-nitrosobis(2-hydroxypropyl)amine (BHP) caused carcinogenic effects in adult Syrian golden hamsters at doses as low as 1/40 of the LD50. The tumor spectrum decreased at lower doses, which affected the pancreas more strongly than the liver, whereas higher doses exhibited a more pronounced hepatocarcinogenicity and also induced tumors in the respiratory tract, gallbladder, kidney, and vagina. These results demonstrated a potent pancreatic carcinogenic effect of

BHP at the lowest dose level. Hence, the presence of BHP in the environment, even in small quantities, should be regarded as a potential hazard to human health. (Author abstract) (9 Refs)

REVIEWS AND OTHER RELATED STUDIES

42. CELL SURFACE GLYCOPROTEIN MARKERS FOR NEOPLASIA.

Bhavanandan VP, Davidson EA
Dept. Biological Chemistry, Milton S. Hershey Medical Center, Hershey, PA, 17033
Methods Cancer Res; 19:53-105 1982

Glycoproteins that serve as cell surface markers of neoplasia are described biochemically, in relation to viral transformation, and for various animal and human cells, and the methods employed are reviewed. The animal tumors and derived cell lines discussed include the following: neuroblastoma, melanoma, ascites, hepatoma, mammary carcinoma, lung carcinoma, and leukemias and lymphomas. Glycoprotein cell surface markers in human cells are reviewed in relation to melanoma, mammary carcinoma, lung carcinoma, colon carcinoma, ovarian carcinoma, and neuroblastoma. Metabolic labeling, isolation, purification, mapping, and structural analysis techniques applied to glycoproteins are reviewed. Future studies in this field will probably take advantage of improved methods such as isoelectric focusing gels, lectin affinity chromatography, and monoclonal antibodies. Ultimately the metabolic and genetic origin of each macromolecule must be determined. In the meantime, glycoprotein cell surface marker studies may be expected to contribute to diagnostic and immunologic approaches to management of disease. (313 Refs)

43. TOXICOLOGY OF N-NITROSO COMPOUNDS.

Coulston F, Olajos EJ
Albany Medical Coll., Albany, NY, 12208
Ecotoxicol Environ Saf; 6(1):89-96 1982

Toxicology of N-nitroso compounds is discussed with respect to formation, carcinogenic effect of precursor amino compounds and nitrite, and significance to man. The potential nitrosation of drugs which are amine or amide derivatives or drug metabolic conversion products containing an amino group is of interest. Experimental evidence that N-nitroso compounds can be formed in vivo is reviewed; however, only a few studies have involved nitrosation conditions simulating those in the environment or in actual animal or human conditions. Standardized in vitro nitrosation assays that more accurately define conditions under which biological nitrosation occurs in the mammalian stomach would enhance our knowledge of in vivo nitrosation. The relationship between N-nitrosation, mutagenicity, and carcinogenicity based on previously reported data of relative in vitro nitrosatability of certain drugs, the mutagenicity of nitrosation products, and the carcinogenicity of the parent compounds when fed to rats concurrently with nitrite is tabulated. Very large differences between nitrosatability of different drugs are evident, establishing the nitrosation assay as a potentially useful screening procedure. A parallel relationship between nitrosatability of various drugs and mutagenicity is demonstrated. Presently, no evidence exists concerning the carcinogenic effect of N-nitroso compounds derived from drugs that are known to undergo nitrosation or to which man has been occupationally exposed. In vitro nitrosation studies have defined potential nitrosatable precursors and the conditions necessary for nitrosation. In vivo tests, with low levels of precursor amino compounds and/or nitrite, reveal levels of N-nitroso derivatives that are not in excess of low background levels. (31 Refs)

44. TRACE METALS AND DISEASES.

Yamane Y, Sakai K

Faculty Pharmaceutical Sciences, Chiba Univ., Yayoi-cho 1-33, Chiba 260, Japan

Yuki Gosei Kagaku Kyokai Shi; 39(11):1105-1113 1981

Trace metal diseases (eg acrodermatitis enteropathica and Menkes' kinky-hair disease), diseases that cause abnormalities in metabolism of essential trace metals (eg Wilson's disease, cystic fibrosis, and hemochromatosis), assays of trace metals in biological fluids as diagnostic or prognostic aids in patients with cancer, and toxic trace metals were discussed. There are many influences that trace metals have on cancer. For example, pernicious anemia often accompanies various serious types of cancer and is related to iron, copper, and cobalt. Most patients with bronchial or some other lung cancers or transverse colon cancer have decreased serum levels of zinc, but patients with breast cancer or melanoma do not have decreased levels of zinc. Patients with primary osteosarcoma have lower copper/zinc ratios than normal subjects, and patients with metastatic osteosarcoma have copper/zinc ratios higher than normal subjects, suggesting a way to differentiate the two types of osteosarcoma. Compared to normal subjects, patients with breast cancer have 6-7x higher levels of total iron in breast tissue, patients with lung cancer have one fifth of the normal level of total iron in lung tissues, and patients with cancer of the transverse colon have normal levels of total iron in the colon tissue. Other studies have indicated the carcinogenic potential of toxic trace metals. (63 Refs) (In JPN)

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NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

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Watson DH, Lindsay DG
Food Science Div., Ministry of Agriculture, Fisheries, and Food, Great Westminster House, Horseferry Road, London SW1P 2AE, England
J Sci Food Agric; 33(1):59-67 1982

37. PITUITARY AND STEROID HORMONES IN RADIATION-INDUCED MAMMARY TUMORS.
Shellabarger CJ
Medical Dept., Brookhaven National Lab., [illegible]pton, NY, 11973
Banbury Rep; 8:339-351 1981

38. ASPERGILLUS NIDULANS: SYSTEMS AND RESULTS OF TESTS FOR CHEMICAL INDUCTION OF MITOTIC SEGREGATION AND MUTATION. I. DIPLOID AND DUPLICATION ASSAY SYSTEMS. A REPORT OF THE U. S. EPA GENE-TOX PROGRAM.
Kafer E, Scott BR, Dorn GL, Stafford R
Dept. Biology, McGill Univ., 1205 Ave. Docteur Penfield, Montreal H3A 1B1, Canada
Mutat Res; 98(1):1-48 1982

OTHER REVIEWS IN CARCINOGENESIS

39. MATHEMATICAL MODELS OF THE CELL CYCLE WITH A VIEW TO TUMOR STUDIES.
Bertuzzi A, Gandolfi A, Giovenco MA
Centro di Studio dei Sistemi di Controllo e Calcolo Automatici del C.N.R., Via Eudossiana 18, 00184 Rome, Italy
Math Biosci; 53(3/4):159-188 1981

40. NEOPLASMS IN DOMESTIC ANIMALS: A REVIEW OF EXPERIMENTAL AND SPONTANEOUS CARCINOGENESIS.

Madewell BR

Section Clinical Oncology, Dept. Veterinary Surgery, Univ. California, Davis, CA, 95616

Yale J Biol Med; 54(2):111-125 1981

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SEPTEMBER, 1982

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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PREVALENCE OF GI CANCER IN HUMAN POPULATIONS

1. CANCER PATTERNS IN TRANSKEI.

Rose EF, Fellingham SA
Natl. Res. Inst. for Nutritional Diseases, South African Medical Res. Council, P.O. Box 192, East London 5200, South Africa
S Afr J Sci; 77(12):555-561 1981

During 1965-1969, 4, 247 malignant tumors were diagnosed in Transkei hospitals, giving standardized rates of 60 and 40 per 100,000 per yr for males and females, respectively. The cancers were analyzed according to relative frequency, age distribution of common cancers and geographical pattern. Cancers of the esophagus, mouth, liver, uterine cervix and breast were the specific neoplasms analyzed. This study dealt with a basically rural community having little communication with urban conditions and may serve as a baseline study for comparisons of cancer patterns already established in urban communities. The pattern of cancer incidence in Transkei is changing and may be a reflection of breakdown of age old taboos and changing social conditions. Similarities were found in the geographical distribution of esophageal and oral cancer in both sexes and in females between hepatic and cervical cancer and also between cancers of the breast and esophagus. (20 Refs)

2. PRECURSOR LESIONS OF OESOPHAGEAL CANCER IN HIGH-RISK POPULATIONS IN IRAN AND CHINA.

Munoz N, Crespi M, Grassi A, Qing WG, Qiong S, Cai LZ
Analytical Epidemiology Program, Div. Epidemiology and Biostatistics, International Agency for Res. on Cancer, 150 Cours Albert-Thomas 69372, Lyon Cedex 2, France
Lancet; 1(8277):876-879 1982

To determine the prevalence of precursor lesions of esophageal cancer in Linxian, People's Republic of China, which has an extremely high incidence of esophageal cancer, 527 subjects were interviewed by a questionnaire about exposure to suspected risk factors. They also underwent esophagoscopy, cytology, and biopsy. 84% had a chronic esophagitis which had similar endoscopic and histological characteristics to that reported in Iran. The esophagitis was accompanied by atrophy of the epithelium in 10% of these subjects and by dysplasia in 8%. Reexamination of 20 selected subjects 1 year later showed progression of the esophagitis to atrophy and dysplasia in 4 individuals and to cancer in 4 others. The surveys in Iran and China suggest that the natural history of esophageal cancer starts with an esophagitis which, in a few individuals, progresses to atrophy and dysplasia of the epithelium and finally to cancer. Thermal injury resulting from the drinking of very hot beverages, physical injury caused by ingesting very coarse food, and deficiencies of riboflavin, vitamin A, and zinc are proposed as risk factors for these precursor lesions. (Author abstract) (17 Refs)

3. AN ASSESSMENT OF CANCER MORTALITY IN GREATER BOMBAY.

Jussawalla DJ, Yeole BB, Natekar MV
Cancer Registry Div., Indian Cancer Society, E. Borges Marg, Parel, Bombay 400012, India
Indian J Med Res; 75:68-82 1982

Cancer was found responsible for approx 3.6% (2.2% males and 1.4% females) of the total number of deaths occurring in Greater Bombay. It was the ninth and eighth commonest cause of death in males and females respectively, in the city. When the mortality rate was examined by age-groups, cancer ranked as the fifth leading cause of death in men and the fourth in women, in those aged 45 and above. The av annual age-adjusted death rate for all sites, was 91.6 in males and 74.8 in females per 100,000 population. Mortality increased with advancing age in both sexes. The truncated death rates for females were found to be higher than for males; thus between the ages of 25 and 54, female deaths exceeded the males, perhaps because of the large number of fatalities caused by cervical and breast cancers at these ages. Around 55, the curves for men and women intersected, following which the male rates were seen to rise steeply, due to the increasing incidence of lung, esophageal and prostatic cancers in men above that age. The common sites leading to death from cancer appeared to be the lung, esophagus, larynx, stomach and prostate in males and breast, cervix, ovaries, esophagus and the stomach in females. Gastrointestinal cancers were a major cause of death in both sexes. (Author abstract) (14 Refs)

4. EPIDEMIOLOGY OF CARCINOMA OF THE COLON AND RECTUM IN IRELAND: MORTALITY ANALYSIS.

Habba SF, Daly L, Doyle JS
St. Laurence's Hosp., Dublin 7, Ireland
Ir J Med Sci; 151(1):6-11 1982

Mortality patterns of cancer of the colon and rectum in Ireland are compared with those of the rest of the world and with respect to age, sex, and geographical distribution within Ireland. Mortality data from the reports on vital statistics (1950-1976) and unpublished data from the Central Statistic Office were used for calculations. International comparisons are based on World Health Organization publications. Time trends were calculated using the indirect method of standardization with 1975 age and sex specific rates chosen as standard, and a standardized mortality ratio was calculated for each year from 1950-1976 using the population figures obtained from the latest census. Geographic variation analysis was based on the combined mortality data from 1973-1975. Even after standardization, Ireland maintains its position with the highest incidence of mortality from malignant neoplasms of the intestine excluding the rectum in males and the second highest in females. The study confirms the continual rise in mortality from cancer of the colon (excluding rectum) in contrast with the trends in England and Wales; the need for early detection of these carcinomas is stressed. (7 Refs)

5. EPIDEMIOLOGY AND EVOLUTION OF GASTRIC CANCER.

Li Voti P
Via Principe di Villafranca, 99, 90141 Palermo, Italy
Minerva Chir; 36(23/24):1709-1712 1981

Between 1975-1976, gastric cancer (GC) mortality was 28.2/100,000 inhabitants in Italy; 2.90% of the total mortality, 14.2% of the total mortality because of tumors, and 42.93% mortality because of tumors of the digestive tract. Incidence of the GC was highest in the province of Emilia-Romagna (199) and Toscana (169) in the central part of the country, and lowest in Sardegna (27) and Puglie (29) in the south. GC frequency is decreasing in Italy by 16.5%, after a peak was reached in 1960-1969. The relationship between GC and nutrition, age, sex, and genetic factors (blood group) were discussed. Different gastric pathologies like atrophic gastritis, giant hypertrophic gastritis (Menetriere's disease), gastric polyposis, and previous gastric resection increase the probability of GC. Canceration of gastric epithelium is very slow. Span of time between appearance of early cancers and appearance of symptoms is slow too, time can vary, but is basically unknown. Survival for patients with GC who were not cured was 2-147 mo after the symptoms had started or 1-145 after the diagnosis. (12 Refs) (In ITA)

6. CANCER IN THAILAND: LESSONS FOR CANCER CONTROL.

Miller DG, Somboocharoen S

Strang Clinic, Preventive Medicine Inst., 55 East 34th St., New York, NY, 10016

Prev Med; 11(2):232-239 1982

Patterns of neoplasia encountered in Thailand are discussed and the implications of the cancer control program of Thailand for cancer control in the United States are reviewed. Cancer was the sixth most common cause of mortality in Thailand in 1970. By 1977 it ranked third after accidents and cardiopulmonary disease. Cancer patients in Thailand, as elsewhere, utilize a disproportionately large fraction of available medical care. In 1975, liver, lung, and stomach in the male and cervical, breast, and liver in the female were the most common malignancies reported by 85 collaborating rural hospitals. In contrast, the most common cancers in urban Thais included nasopharyngeal, oral and lung in the male, and cervical, oral and lung in the female. The Thai program for cancer control indicates that (1) there is no effective cancer control without early diagnosis; (2) the detection of early cancer requires special effort; (3) the premise that screening programs should be directed exclusively at asymptomatic patients should be reexamined; (4) screening programs without follow-up are counterproductive; (5) screening programs will be most successful when linked with ongoing activities that represent a desired social or medical benefit; (6) totally integrated health care services offer the best opportunity for cancer control; (7) Cancer control services should be incorporated into programs offering comprehensive health care; (8) volunteer resources should be tapped to the extent that they are available; (9) environmental hazards should be eradicated; and (10) commercial marketing practices may affect cancer control. (8 Refs)

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN GI CARCINOGENESIS

7. 'CIVILIZATION-ASSOCIATED' DISEASES IN EUROPE AND INDUSTRIAL COUNTRIES OUTSIDE OF EUROPE: REGIONAL DIFFERENCES AND TRENDS IN MORTALITY.

Junge B, Hoffmeister H

Inst. Social Medicine and Epidemiology, Federal Health Office, Postfach, D-1000 Berlin 33, W. Germany

Prev Med; 11(2):117-130 1982

Death rates and changes in death rates from 1958-1976 for the leading causes of mortality, including cancer, are described for 26 countries. The United States (US), Canada, and Australia experienced a reduced rate of stomach cancer mortality compared to Japan, Portugal, and Eastern European countries. Mortality from lung cancer (average of all countries considered) rose by 40 deaths per 100,000 for men and by 10 deaths per 100,000 for women. Lung cancer rates in England and Wales, the US, Denmark, Canada and Australia increased three to four-fold in 18 yr. (35 Refs)

8. MORTALITY STATISTICS AMONG ATOMIC BOMB SURVIVORS IN HIROSHIMA PREFECTURE, 1968-1972.

Kurihara M, Munaka M, Hayakawa N, Yamamoto H, Ueoka H, Ohtaki M

Dept. Epidemiology and Social Medicine, Res. Inst. for Nuclear Medicine and Biology, Hiroshima Univ., 2-3 Kasumi 1-chome, Minami-ku, Hiroshima 734, Japan

J Radiat Res (Tokyo); 22(4):456-471 1981

Mortality among the approx 160,000 atom bomb survivors in Hiroshima during the period 1968-72 due to selected causes of death, including malignant neoplasms, is discussed. In terms of all causes of death, the relative risk of survivors was 0.913, which is significantly lower than for the non-exposed population. The risk of survivors for malignant neoplasms, however, was 16% higher than for non-exposed individuals. The risk of some neoplasms was significantly elevated in the survivor population: leukemia, lymphosarcoma, reticular cell sarcoma, and cancer of the large intestine, testis, ovary, and larynx. Others neoplasms, such Hodgkin's disease, carried a lower risk. Among non-neoplastic causes of death, diseases of the blood and blood-forming organs, hypertensive diseases, and others are at a significantly higher risk in the exposed group whereas senility, gastroenteritis, and accidents are all significantly lower. (11 Refs)

9. THE UTILITY OF REGIONAL CANCER MORTALITY DATA FOR IDENTIFYING OCCUPATIONS AT HIGH RISK.

Kraus JF, Franti CE, Newman B

Sch. Public Health, Div. Epidemiology, Southern Occupational Health Center, Univ. California, Room 76-078, Los Angeles, CA, 90024

Scand J Work Environ Health; 8(Suppl1):65-71 1982

Relation of the excess in cancer death (CD) rates in Sacramento County with specific occupations was investigated and the utility of census data for such analysis is discussed. The analysis of CD by occupation was limited to white males, usual residents of Sacramento County (RSC). The CD certificates examined were restricted to persons whose age at death was from 40-64 yr. During the 1969-1977 period, 1,997 CD among male RSC were observed. The observed and expected numbers of CD and the standardized mortality ratio (SMR) for each of the occupational groups are presented. Technicians, construction craftsmen and cabinet makers, metal craftsmen, and nonfarm laborers showed SMR greater than 140. SMR of less than 70 was found for lawyers, physicians, scientists, teachers, social and religious workers, and sales clerks. Construction craftsmen and drivers exhibited excessive SMR in older age group (55-64 yr old). Low SMR were found for teachers, social/religious workers, and sales clerks in both age groups and for young lawyers, physicians, and scientists. SMR for greater than 140 by occupational category and cancer site is presented. The SMR for metal craftsmen and engineers were excessive for cancer of the esophagus and CNS. Construction workers and drivers had high SMR for cancer of the esophagus and skin. Technicians showed a high SMR for cancer of the bowel and CNS. Several occupational categories showed low SMR for cancer of the lung, including teachers, social/religious workers, writers, artists, architects, clerical workers, station engineers, mechanics, foremen, operatives, farmers, police, fire, and safety officers. Clerical workers and operatives had low SMR for leukemia and lymphoma. (9 Refs)

10. THE CARCINOGENIC EFFECT OF AROMATIC AMINES: AN EPIDEMIOLOGICAL STUDY ON THE ROLE OF O-TOLUIDINE AND 4,4'-METHYLENE BIS(2-METHYLANILINE) IN INDUCING BLADDER CANCER IN MAN.

Rubino GF, Scansetti G, Piolatto G, Pira E
Inst. Occupational Health, Turin Univ., CTO- Via Zuretti, 29-10126 Torino, Italy
Environ Res; 27(2):241-254 1982

Cause-specific mortality of 906 workers first employed 1922-1970 in a dyestuff factory in Northern Italy was compared to national figures; a marked excess of bladder cancer was observed (36 observed vs 1.23 expected deaths). The mean latent period was 25 years. The excess was higher among those with longer duration of exposure. Some excess of mortality from lung cancer, laryngeal cancer, and esophageal cancer was also found, but a clear explanation could not be provided regarding the causal role of aromatic amines. Mortality from bladder cancer was very much higher among those exposed in benzidine and naphthylamines manufacture as compared to those only exposed in use or intermittent contact. Excess bladder cancer was also very high among workers in fuchsin manufacture. There is evidence that O-toluidine and 4,4'-methylene bis(2-methylaniline) should be implicated in such excess mortality. Caution in handling these compounds is therefore suggested and the need for further studies to confirm such findings is stressed. (Author abstract) (19 Refs)

11. RESTRICTED COHORT STUDY DESIGNS.

Oakes D, McDonald JC
TUC Centenary Inst. Occupational Health, London Sch. Hygiene and Tropical Medicine, Univ. London, Keppel St. (Gower St.), London WC1E 7HT, England
Scand J Work Environ Health; 8(Suppl1):30-33 1982

Effects of three types of restriction (selection for employment, survival at work, and susceptibility to the effects of exposure) were studied using data from a large cohort of Quebec chrysotile miners and millers comprising all 11,379 persons born between 1891-1920 who had worked for 28 days or more in this industry. Results of the three restricted analyses (deaths from pneumoconiosis, malignant disease of the respiratory and digestive tract among males), preceded by the case-referent analysis of the full cohort, in which there were 4,463 male deaths, are presented. (10 Refs)

12. MORTALITY PATTERNS OF ROCK AND SLAG MINERAL WOOL PRODUCTION WORKERS: AN EPIDEMIOLOGICAL AND ENVIRONMENTAL STUDY.

Robinson CF, Dement JM, Ness GO, Waxweiler RJ
Div. Surveillance, Hazard Evaluations, and Field Studies, Natl. Inst. Occupational Safety and Health, Center Disease Control, Cincinnati, OH, 45202
Br J Ind Med; 39(1):45-53 1982

An epidemiological and environmental study of rock and slag mineral wool production workers was undertaken at a plant that has been in operation since the early 1900s. Size characteristics of fibers produced by each process at the plant and data from industrial hygiene surveys were used to evaluate current and past exposures. These data suggest that the av historical airborne fiber concentration probably did not exceed 2.5 fibers/cc before 1935 and 1.0 fiber/cc after 1935. A retrospective cohort mortality study was designed to assess mortality patterns. Detailed occupational histories were compiled on all plant employees. All jobs in the plant were assigned to one of eight potential exposure categories to assess the extent and severity of mineral wool exposure and the effect of other significant exposures on employee mortality. Findings included an increase in the number of deaths due to cancer of the digestive system and non-malignant respiratory disease among workers who had over 20 yr exposure to mineral wool or who had survived 20 yr since their first exposure to mineral wool. These findings are not inconsistent with those of Enterline's (Symposium on Biological Effects of Mineral Fibres, Lyon, France, September 1979) in the Thermal Insulation Manufacturers' Association's mortality study of men employed in four mineral wool plants. (Author abstract) (32 Refs)

13. A COHORT STUDY ON MORTALITY AMONG LONG-TIME EMPLOYED SWEDISH CHIMNEY SWEEPS.

Hogstedt C, Andersson K, Frenning B, Gustavsson A
Dept. Occupational Medicine, Natl. Board Occupational Safety and Health, S-171 84 Solna, Sweden
Scand J Work Environ Health; 8(Suppl1):72-78 1982

A cohort study was performed on all members of the Swedish Chimney Sweeps Union who were active in 1950 or later and who were members for at least 10 yr. A total of 2,071 sweeps were studied; 2,048 were evaluable. Compared to the national av, the mortality of the exposed cohort was significantly increased (230 observed vs 197.6 expected before the age of 80) due to a greater number of deaths from tumors, particularly lung and esophageal cancer, and from nonmalignant diseases of the respiratory system (chronic bronchitis, emphysema, and asthma). The increased overall mortality was higher among those with shorter exposure time, although esophageal cancer and chronic respiratory diseases were more frequent in long-time exposed individuals. The excess mortality was more predominant among men who left the profession before 1965 than among those who were still working that yr or later. Exposure of chimney sweeps could explain the mortality pattern observed in this study, however, cigarette smoking may have been a contributing factor. Exposure to polycyclic aromatic hydrocarbons, nitrogen compounds, arsenic, and asbestos in combination with promotion from exposure to sulfur dioxide probably caused the increased mortality in these men. (21 Refs)

14. MORTALITY AND CANCER MORBIDITY AMONG WORKERS IN THE RUBBER TIRE INDUSTRY.

Delzell E, Lewis J, Monson RR
(c/o Monson) Dept. Epidemiology, Harvard Sch. Public Health, 677 Huntington Ave., Boston, MA, 02115
Am J Industr Med; 2(3):209-216 1981

Mortality and cancer incidence were evaluated retrospectively in 1,792 white men employed at a rubber tire plant between 1954 and 1976. The 1,792 workers had accumulated 26,839 person-yr of follow up. Among men employed for 10 yr or more, overall cancer mortality was approx 19% higher than that expected in Connecticut white males, whereas cancer incidence for all sites combined was similar in the two groups. Excesses in deaths and incident cases for cancers of the buccal cavity and pharynx, large intestine, pancreas, and kidney were observed. The workers also showed excesses in deaths from cancers of the digestive organs and peritoneum and incident cases of cancer of the bronchus and lung. No increase in occurrence of stomach or bladder cancer or of leukemia was seen. Limitations of the data are discussed in terms of interpreting the results. As the workers investigated were young (93% total person-yr less than 65 yr old), and because estimates of cancer excesses were conservative in this study, cancer mortality and morbidity should continue to be monitored in the rubber industry. (15 Refs)

15. CANCER MORBIDITY AMONG WOODWORKERS IN THE U.S. AUTOMOTIVE INDUSTRY.

Swanson GM, Belle SH
Dept. Social Oncology, Michigan Cancer Foundation, 110 East Warren, Detroit, MI, 48201
JOM; 24(4):315-319 1982

In October 1979, concern was expressed about suspected excess cancer among woodworkers in several automobile manufacturing plants of the major automobile corporations located in Detroit. Cancer incidence rates for this group were compared with corresponding data for white males in the Detroit metropolitan area. Determination of standardized morbidity ratios (SMRs) showed significant increases for all types of cancer combined and for colorectal and salivary gland cancer in the study group. Further investigation is required to determine whether occupational exposure is responsible for these increases or if some other etiological mechanism is operating. (Author abstract) (38 Refs)

DIETARY AND DIGESTIVE FACTORS IN GI CARCINOGENESIS

16. DIETARY FIBER AND DISEASE.

Kritchevsky D
Wistar Inst. Anatomy and Biology, Philadelphia, PA
Bull NY Acad Med; 58(3):230-241 1982

The association between dietary fiber and disease is reviewed. Classification of fiber is based on chemical components of the main chain; various fiber classes (pectins, hemicellulose, cellulose, lignin) have different physiological actions in humans. The possible association between levels of dietary fiber and colon cancer and atherosclerosis is discussed. A diet high in complex carbohydrates (high fiber diet) has resulted in reduced serum cholesterol and glucose and also reduced insulin requirements. No directly positive influence of dietary fiber on lipid metabolism and colon cancer has consistently been found. (77 Refs)

17. NUTRITION AND CANCER: MECHANISMS OF GENOTOXIC AND EPIGENETIC CARCINOGENS IN NUTRITIONAL CARCINOGENESIS.

Weisburger JH, Horn C
American Health Foundation, Valhalla, NY, 10595
Bull NY Acad Med; 58(3):296-312 1982

Mechanisms of carcinogenesis are reviewed with regard to type of chemical carcinogen - genotoxic, cocarcinogen, or promoter. Examples and mode of action are given for each. The role of epigenetic agents in nutritionally linked cancers, particularly large bowel or colon cancer, is discussed; specific dietary elements considered relevant through studies in human and animal models are the amount of dietary fat and fiber and mode of cooking. The operation of these elements is through epigenetic mechanisms, which are dose and time dependent. A reduction in dose should lead to lowering of risk, which may eventually be applied to humans through dietary adjuvant therapy. (71 Refs)

18. RELATIONSHIP BETWEEN VITAMIN E AND CANCER - FACTS, NOT FANCY.

Ellison NM
Dept. Medical Oncology, Geisinger Medical Center, Danville, PA
Cancer Bull; 34(1):43-44 1982

The roles of vitamin E in inhibition of carcinogenesis and amelioration of conventional cancer treatment toxicity are discussed. Studies with mammalian models suggest that vitamin E may act as a protector against radiation-induced cellular damage and as a radiosensitizer in cancer treatment. The conflict between these antagonistic functions must be resolved. Vitamin E has been shown to ameliorate the toxic effects of doxorubicin in animal models without adversely affecting antineoplastic activity. Vitamin E may also act as an inhibitor of stomach cancer by inhibiting the reactions converting nitrites and nitrates to nitrosourea; possible prevention of gastric cancer by steady consumption of vitamin E and C has been suggested. Vitamin E, an antioxidant with the ability to inhibit free-radical-induced lipid peroxidation, may have some role in human carcinogenesis and cancer treatment, but evidence to support such a role is insufficient. (16 Refs)

19. ASSESSING HUMAN EPIDEMIOLOGIC DATA ON DIET AS AN ETIOLOGIC FACTOR IN CANCER DEVELOPMENT.

Enstrom JE
Sch. Public Health, Univ. California, Los Angeles, CA
Bull NY Acad Med; 58(3):313-322 1982

Assessment of the relationship between diet and cancer is reviewed. Epidemiology of cancer among human populations consists of randomized, controlled trials based on interpretation of naturally occurring phenomena. The strongest epidemiologic data relating diet to cancer are geographic correlations between such factors as per capita fat consumption and age adjusted colon and breast cancer rates. Weaknesses exist in such correlation: large variation in colon cancer rates occurs within the United States (US), even when fat intake remains constant. Studies of Japanese who migrate from Japan to the US provide another form of epidemiologic evidence for a correlation between diet and cancer. Japanese emigrants in the US have increased rates for colon and breast cancer as compared to native Japanese; such selective use of epidemiologic data is partially contradicted by other data which indicate that the overall total cancer rate among Japanese Americans remains unchanged, with a total death rate lower than that of native Japanese. Specific populations which maintain diets different from the average American diet are discussed, using as examples Mormons and Mexican Americans. No data has demonstrated any specific relationship between diet and cancer rate. (26 Refs)

20. MEAT AND FAT CONSUMPTION AND CANCER MORTALITY: A STUDY OF STRICT RELIGIOUS ORDERS IN BRITAIN.

Kinlen LJ
Cancer Res. Campaign, Cancer Epidemiology Res. Group, Univ. Oxford, Radcliffe Infirmary, Oxford, England
Lancet; 1(8278):946-949 1982

The close correlations between mortality from breast and colorectal cancers and the per-capita consumption of meat or fat in different countries suggest that these dietary items may be involved in the etiology of these neoplasms. To investigate further these possible relations a study has been conducted of cancer mortality between 1911 and 1978 in two groups of enclosed religious orders for women: one of 1,769 nuns who eat no meat and one of 1,044 nuns who eat little meat. Mortality from breast and colorectal cancer was not significantly lower in either group than in the general population. It is difficult to evaluate the small reduction in breast cancer mortality in the no-meat group because of the wide confidence limits. An unexpected finding was an excess mortality from esophageal cancer in both groups. These findings concern women who reduced their meat consumption in adult life: it is suggested that they are compatible with the evidence put forward to support a role for fat or meat intake in causation of breast cancer if dietary influences in pre-adult life are important. The findings on colorectal cancer point to the etiological importance in this disease of aspects of diet other than fat or meat intake. (Author abstract) (34 Refs)

21. FAECAL MUTAGENESIS AND COLONIC CANCER.

Askew AR, Ward M, Green MK, Reibelt LD
Dept. Surgery, Royal Brisbane Hosp., Herston 4029, Australia
Aust NZ J Surg; 52(1):27-29 1982

The incidence of fecal mutagens has been evaluated using the Ames Test in 16 patients with proven colon cancer and 35 volunteers with no symptoms referable to the colon and a negative hemoccult test. Twenty-five percent of the cancer patients, and 20% of the volunteers had mutagen positive feces. These results suggest that the incidence of fecal mutagens in patients with colon cancer is similar to that found in a population with a high risk of developing colonic neoplasms. (Author abstract) (8 Refs)

22. NATURAL OCCURRENCE OF MONILIFORMIN TOGETHER WITH DEOXYNIVALENOL AND ZEARALENONE IN TRANSKEIAN CORN.

Thiel PG, Meyer CJ, Marasas WF
Natl. Res. Inst. Nutritional Diseases, South African Medical Res. Council, Tygerberg 7505, Republic of South Africa
J Agric Food Chem; 30(2):308-312 1982

Fusarium infected ears of corn grown in a high human esophageal cancer incidence region were assayed for deoxynivalenol (DON), moniliformin (MF), zearalenone (ZL), T-2 toxin, and diacetoxyscirpenol. Cultures of F graminearum, F verticillioides, and F sacchari var subglutinans from the corn were raised in vitro and assayed for the chemicals. Only DON, MF, and ZL were found in the corn. F graminearum produced DON and ZL. F sacchari produced MF, and F verticillioides produced none. (24 Refs)

OTHER ETIOLOGIC FACTORS IN GI CARCINOGENESIS

23. FAMILY INCIDENCE OF CARCINOMA OF THE COLON AND RECTUM IN NORTH-EAST SCOTLAND.

Duncan JL, Kyle J
(c/o Kyle) Gastroenterology Res. Unit, Ward 32, Royal Infirmary, Foresterhill, Aberdeen AB9 2ZB, Scotland
Gut; 23(2):169-171 1982

Family histories were obtained from 50 patients with adenocarcinoma of the colon or rectum in northeast Scotland. A comparable control group was similarly interviewed and in each group the case notes of the first degree relatives were studied where possible. Eight (16%) of the patients with cancer of the colon or rectum had a close relative with intestinal cancer compared with one (2%) of the control group. The patients with a positive family history of cancer of the large intestine did not have a higher proportion with adenomatous polyps nor were they younger than those patients with no such family history. (Author abstract) (12 Refs)

24. MISCELLANEOUS DISORDERS. THE GASTROINTESTINAL TRACT.

Candy DC, Howard FM, McNeish AS
Univ. Birmingham Inst. Child Health, Nuffield Building, Francis Road, Birmingham B16 8ET, England
Clin Gastroenterol; 11(1):207-229 1982

Miscellaneous disorders of the gastrointestinal tract and genetic and familial factors are discussed. In two families from Liverpool, 24 cases of esophageal carcinoma were associated with tylosis. Several families with a high incidence of gastric carcinoma have been described. The blood group A phenotype confers a 10-20% elevation in gastric carcinoma rate. Small intestinal primary carcinoma does not occur in geographical or population clusters, suggesting that genetic or environmental influences are unimportant. Underlying chronic small intestinal disorders such as celiac disease and Crohn's disease predispose small bowel malignancy; such disorders appear to run in families. (157 Refs)

25. FAMILIAL POLYPOSIS COLI AND PERIAMPULLARY MALIGNANCY.

Harned RK, Williams SM
Dept. Radiology, Univ. Nebraska Medical Center, 42nd and Dewey Ave., Omaha, NE, 68105
Dis Colon Rectum; 25(3):227-229 1982

Patients with polyposis coli have an increased risk of developing periampullary malignancies, particularly if duodenal polyps are present. Since periampullary neoplasms occur, on the av, 15 yr following the initial diagnosis of colonic polyps, periodic follow-up radiologic studies of the upper gastrointestinal tract are necessary in the management of polyposis coli. (Author abstract) (21 Refs)

26. GARDNER'S SYNDROME: SIX GENERATIONS.

Palmer TH
431 State St., Bangor, ME, 04401
Am J Surg; 143(4):405-408 1982

A family of 68 members in six generations has been investigated, and thus far 23 of these have had colorectal polyposis, cancer or both. Many of the 23 have had a variety of soft tissue lesions, occult osteomas of the mandible, and dental abnormalities. Six of nine siblings in the proband's immediate family had diffuse colorectal polyposis and soft tissue lesions, as have 4 of their 20 children. One of three members of the most recent generation has polyposis and skin lesions. Retrospectively, 2 of the proband's 18 maternal cousins had colorectal polyposis or cancer, as did five of six siblings in her mother's generation. Four of nine siblings in the previous generation died from colon cancer, and so did their father. In the first three generations cancer was prevented in only 1 of 10 patients. Two of 13 in the later three generations thus far have died from colorectal cancer. Both coloproctectomy and colectomy with preservation of the rectum have been utilized in the patients in this study. Lifelong follow up is underway for those whose rectum has not been removed. (Author abstract) (24 Refs)

27. POLYPS AND CARCINOMA OF THE COLON.

Sivak MV

Section Endoscopy, Dept. Gastroenterology, Cleveland Clinic Foundation, 9500 Euclid Ave., Cleveland, OH, 44106

Primary Care; 8(2):335-347 1981

The treatment of choice for carcinoma of the colon is surgical resection, although surgical cure rates over the past decade have not changed appreciably and remain at 30-50%. The relation of colonic adenoma to adenocarcinoma, usually termed the polyp-cancer sequence, is emphasized. Classification of polyps, the polyp-cancer sequence, risk factors for carcinoma of the colon, and screening for carcinoma of the colon are discussed. (18 Refs)

28. PHENOTYPIC VARIATION IN HEREDITARY ADENOMATOSIS: UNUSUAL TUMOR SPECTRUM.

Lynch HT, Ruma TA, Albano WA, Lynch JF, Lynch PM

Dept. Preventive Medicine, Creighton Univ. Sch. Medicine, 2500 California St., Omaha, NE, 68178

Dis Colon Rectum; 25(3):235-238 1982

Familial adenomatous polyposis coli is a heterogeneous disease with respect to genetics as well as its colonic polyposis and cancer phenotype. The authors report a family with variation in phenotypic expression of polyps ranging from isolated polyps to florid carpeting of the entire colonic mucosal surface. In addition to early-onset colonic cancer, a patient with isolated polyps had a seminoma and subsequently developed gastroesophageal cancer. His son, also with isolated colonic polyps, manifested a pararectal rhabdomyosarcoma. The significance of these variations can only be assessed fully through the study of cancer of all anatomic sites in many additional families. (Author abstract) (6 Refs)

29. CARCINOMA OF THE OPERATED STOMACH.

Schacht U, Borchard F, Kniemeyer H, Palomba PP

Chirurgische Klinik A, Moorenstrasse 5, 4000 Dusseldorf, W. Germany

Aktuel Chir; 17(2):63-65 1982

Seventy-one patients (66 men, 5 women; av age, 62), who had surgery because of benign gastric lesions and lesion-free periods greater than 5 yr before carcinoma of the gastric stump (CGS) was diagnosed, were included in this study. Sixty-six of the patients had the CGS and 5 had carcinoma at the site of gastroenterostomy. The av lesion-free period between the benign and malignant lesions was 24 yr. Of the 69 patients who underwent surgery, 22 had radical resection, 19 had palliative resection, and 28 had laparotomy. Surgical mortality was 19.1%. Survival was 50% after 3 mo and 5.2% after 5 yr. Five-yr survival of the patients who underwent radical surgery was 18.2%, or 26.7% of those who survived the surgery. Histologic examination of the gastric stumps did not indicate any significant difference between obligatory or facultative bile reflux. Incidence of the CGS was increased when the primary lesion was a duodenal ulcer. Relationships between the CGS and type of primary surgery, alkaline reflux, chronic gastritis, acidity, and exogenous carcinogens were discussed. (17 Refs) (In GER)

30. CANCER OF GASTRIC STUMP AFTER GASTRODUODENAL RESECTION DUE TO BENIGN ULCER.

Saegesser F, Macarone-Palmieri R

Service e Chirurgie A, Centre Hospitalier Universitaire Vaudois, 1011 Lausanne, Switzerland

Minerva Chir; 36(23/24):1715-1718 1981

Different types of surgery are used for the resection of peptic ulcers. All of them have certain mortality, mechanical and metabolic disturbances, and lithogenous effect. Cancer of gastric stump (CGS) is another complication that can occur after gastroduodenal resection (RGD). Follow-up was easier in a small rural Canton of Vaud. Between 1929-1960, majority of patients had RGD with Billroth II (type Hofmeister-Finsterer) reconstruction, [71% of them had duodenal ulcer (DU), 23% had gastric ulcer (GU), and 6% had both] Probable relationship between permanent biliary-pancreatic reflux (BPR) in the resected stomach (pH 6) and the canceration of the gastric stump was discussed. Between 1956-1978, 1,417 gastric surgeries were performed due to malignant gastric tumors. Forty-six were found in patients who had previous surgery due to benign peptic ulcer. Of the 46 patients, 6 had gastric cancer 33 yr after first surgery, 1 had the CGS 7.5 yr after RGD and Billroth I, and 39 (37 men, 2 women; av age 61.8 yr) had the CGS 8-53 yr after RGD and Billroth II due to the GU in 8 of the patients and to the DU in 31. Location of the CGS was in the region of anastomoses in 22 of the patients. Ten patients had total invasion of the gastric stump, and 7 had CGS in gastroesophageal region. Incidence of the CGS increases with time and reaches max 15-30 yr after first surgery. Of the 39 patients with the CGS, 26 had surgery more than 5 yr ago, 14 of them had radical surgery, 1 died immediately after surgery, 6 are living without sign of relapse, 7 died 9 mo to 3.5 yr later. (no Refs) (In ITA)

31. POLYPS IN THE GASTRIC STUMP.

Dirschmid K, Vogel W, Troyer E

Institut fur Pathologie, Landeskrankenhaus, A-6807 Feldkirch (Vorarlberg), Austria

Leber Magen Darm; 11(3):136-138 1981

A retrospective study of the occurrence of polyps of the gastric stump among 1,292 patients after gastric surgery is reported. The occurrence rate was 0.7%, comparable to that for stomachs not undergoing surgery. Kinds of polyps included focal hyperplasia (1), hyperplasiogenic polyp (6), adenoma (10), border-line lesion (1), and early carcinoma (2). Although the small number of patients with polyps precludes analysis of subgroups, about one-third of the polyps were cancerous or precancerous. (15 Refs) (In GER)

32. AGE DISTRIBUTION OF RIGHT- AND LEFT-SIDED COLORECTAL CANCERS.

Slater G, Papatestas AE, Tartter PI, Mulvihill M, Aufses AH

Dept. Surgery, Mount Sinai Medical Center, One Gustave L. Levy Place, New York, NY, 10029

Am J Gastroenterol; 77(2):63-66 1982

The age distributions in different anatomic areas of the colorectum were compared in 410 patients. The av age for patients with right-sided cancers (71.3 yr) was significantly higher than that for patients with left-sided cancers (67.5 yr). In addition, there was a significantly higher percentage of patients over the age of 70 (mean age of the whole group) in the right colon group as compared with the left colon group. It was concluded that the older age distribution of right-sided cancers might be explained by the delayed effect of an environmental carcinogen in a population with a longer life expectancy. (Author abstract) (27 Refs)

33. THE ASSOCIATION OF REMOTE STREPTOCOCCUS BOVIS BACTEREMIA WITH COLONIC NEOPLASIA.

Friedrich IA, Wormser GP, Gottfried EB
(c/o Wormser) Infectious Diseases Div., New York Medical College, Room 03, Westchester County Medical Center, Valhalla, NY, 10595
Am J Gastroenterol; 77(2):82-84 1982

We prospectively studied five patients with a remote history of Streptococcus bovis bacteremia who had not previously been evaluated for colonic pathology. This study was prompted by several reports of concomitant neoplasia in patients with recent S. bovis bacteremia. The patients were studied at a mean of 32 months after bacteremia. Despite the absence of other signs or symptoms suggestive of bowel disease, a negative test for occult blood in stool and a negative fecal culture for S. bovis, two patients were found to have neoplastic polyps of the colon. These findings suggest that the risk of colonic neoplasia in patients with remote S. bovis septicemia is similar to that found in patients with recent bacteremia, but evaluation of a larger group of these patients will be necessary to establish this risk. (Author abstract) (8 Refs)

INDUCTION OF GI CARCINOGENESIS IN ANIMALS

34. TOXICITY AND METABOLISM OF ACRYLONITRILE.

Sapota A, Chmielnicka J
Zaklad Metabolizmu Substancji Toksycznych, Instytut Medycyny Pracy, ul. Teresy 8, 90-950 Lodz, Poland
Med Pr; 32(1):25-33 1981

Studies in experimental animals and in vitro culture on the toxic effects and metabolism of acrylonitrile (AN) are reviewed. AN was found to be mutagenic for certain strains of Salmonella typhimurium and Escherichia coli. Increased incidence of tumors of the mammary glands, stomach, peripheral nervous system and sebaceous glands of the auditory meatus was found in female rats inhaling AN for 52 wk compared with controls. (40 Refs) (In POL)

35. CARCINOGENICITY OF 2-AMINO-4-(5-NITRO-2-FURYL)THIAZOLE IN RATS BY ORAL AND SUBCUTANEOUS ADMINISTRATION.

Wang CY, Kamiryo Y, Croft WA
Dept. Chemical Carcinogenesis, Michigan Cancer Foundation, 110 E. Watten Ave., Detroit, MI, 48201
Carcinogenesis; 3(3):275-277 1982

Female Fischer rats were divided into two groups and fed either basal diet or basal diet containing 0.166% 2-amino-4-(5-nitro-2-furyl)thiazole for 52 wk followed by basal diet for an additional 16 wk. Out of the 24 rats fed 2-amino-4-(5-nitro-2-furyl)thiazole, 23 had forestomach tumors, 4 had fibroadenomas and 2 had adenocarcinomas in the mammary glands, 2 had renal pelvic carcinomas, 5 had papillomas and 6 had carcinomas in the bladder, and 2 had cutaneous tumors. None of the 10 rats fed basal diet developed tumors. In another study, 2-wk-old Fischer rats of both sexes were injected sc once a wk for the first 8 wk with 2-amino-4-(5-nitro-2-furyl)thiazole at a dose of 10 mg/kg and then 1.4 mg/rat for an additional 46 wk. The control rats were injected with solvent (dimethyl sulfoxide:water, 1:1) only. The experiment was terminated at the end of 58 wk. Malignant fibrous histiocytomas were found in 5 out of 8 male rats and 4 out of 11 female rats, and and angiosarcoma was found in one out of eight male rats injected with 2-amino-4-(5-nitro-2-furyl)thiazole. None of the control rats developed tumors. (Author abstract) (12 Refs)

36. INDUCTION OF COLORECTAL SQUAMOUS CELL CARCINOMAS IN RATS BY DEXTRAN SULFATE SODIUM.

Hirono I, Kuhara K, Yamaji T, Hosaka S, Golberg L

Dept. Carcinogenesis and Cancer Susceptibility, Inst. Medical Science, Univ. Tokyo, Shirokanedai 4-6-1, Minatoku, Tokyo 108, Japan

Carcinogenesis; 3(3):353-355 1982

ACI rats, 15 males and 15 females, were fed a diet containing 1% dextran sulfate sodium for 660 days. Twenty two of 29 surviving rats developed intestinal tumors between 288 and 660 days. Most tumors consisted of papillomas, and four squamous cell carcinomas were also induced, in addition to adenomas and adenocarcinomas. No intestinal tumors were observed in rats of the control group. (Author abstract) (5 Refs)

37. ESOPHAGEAL CARCINOGENESIS IN F344 RATS BY NITROSOMETHYLETHYLAMINES SUBSTITUTED IN THE ETHYL GROUP.

Lijinsky W, Saavedra JE, Reuber MD, Singer SS

Chemical Carcinogenesis Program, NCI-Frederick Cancer Res. Facility, P.O. Box B, Frederick, MD, 21701

JNCI; 68(4):681-684 1982

The carcinogenic activity in male F344 rats of five nitrosomethylalkylamines related to nitrosomethylethylamine has been examined. All rats were tested by administration of controlled doses of the compounds in the drinking water. Nitrosomethylbenzylamine was the most potent carcinogen of the five, causing death of most animals with tumors of the upper gastrointestinal tract (mainly the esophagus) within 6 mo after a total dose of 0.2 mmol. The remaining compounds, all of which can be considered true derivatives of nitrosomethylethylamine, were less potent than nitrosomethylbenzylamine but also induced a high incidence of tumors of the esophagus. Nitrosomethyl-2-phenylethylamine and nitrosomethylneopentylamine were of comparable potency, while nitrosomethyltrifluoroethylamine was considerably less potent, as measured by the time to death with esophageal tumors. Deuterium-labeled nitrosomethylethylamine, in which deuterium replaces hydrogen on the beta-carbon atom of nitrosomethylethylamine, induced a high incidence of esophageal tumors as well as liver tumors after administration of identical doses. Reactions on the beta-carbon atom of nitrosomethylethylamine might be important as well as oxidation at the alpha-carbon atoms in determining carcinogenic effects. (Author abstract) (16 Refs)

MECHANISMS AND MODIFICATIONS OF GI CARCINOGENESIS

38. THE EFFECT OF WARFARIN ON SPONTANEOUSLY METASTASISING COLORECTAL CANCER IN THE RAT.

Mooney B, Serlin M, Taylor I
Dept. Surgery and Pharmacology, Univ. Liverpool, Liverpool, England
Clin Oncol; 8(1):55-59 1982

A study of the effect of warfarin on the natural history of azoxymethane-induced colorectal cancer in the rat has been carried out. Fifty rats were treated with azoxymethane in a dose of 10 mg/kg/wk for 12 wk. They were then divided into two groups. One group act as a control while the other was treated with warfarin (0.2 mg/l drinking water) for 6 wk. Insofar as was possible coprophagy was prevented. Adequate anticoagulation was achieved. The animals were allowed to survive until signs of advanced disease developed. Laparotomy and post-mortem were then carried out. The number of primary colorectal tumors in the warfarin treated group (155) was statistically significantly less than that in the control group (225). The number of lung and liver metastases were also statistically significantly reduced in the warfarin treated group (4) compared to the control group (12). This study suggests that not only does warfarin have antimetastatic properties but apparently inhibits primary tumor growth also. (Author abstract) (16 Refs)

39. GLUTATHIONE S-TRANSFERASE ACTIVITY: ENHANCEMENT BY COMPOUNDS INHIBITING CHEMICAL CARCINOGENESIS AND BY DIETARY CONSTITUENTS.

Sparnins VL, Venegas PL, Wattenberg LW
Dept. Lab. Medicine and Pathology, Univ. Minnesota, Minneapolis, MN, 55455
JNCI; 68(3):493-496 1982

Benzyl isothiocyanate, beta-naphthoflavone, coumarin, alpha-angelicalactone, disulfiram, indole-3-carbinol and indole-3-acetonitrile induced increased (GSH) glutathione S-transferase activity in the liver and small intestine in female ICR/Ha mice. All seven compounds are inhibitors of chemical carcinogenesis. In additional work, several dietary constituents increased GSH S-transferase activity. Consumption of diets containing dried powdered preparations of brussel sprouts, cabbage, coffee beans, or tea leaves resulted in increased GSH S-transferase activity. Mice fed an unrefined diet (Purina Rat Chow) had a higher GSH S-transferase activity than those fed a semipurified diet. The results of the present study indicated that the composition of the diet can alter the activity of an important enzyme system having the capacity to detoxify chemical carcinogens. (Author abstract) (28 Refs)

40. BILE ACIDS: EFFECTS ON ABSORPTION OF 1,2-DIMETHYLHYDRAZINE AND 7,12-DIMETHYLBENZ[A]ANTHRACENE IN THE COLON OF THE RAT AND GUINEA PIG.

Rose RC, Nahrwold DL
Dept. Surgery, Milton S. Hershey Medical Center, Pennsylvania State Univ., Hershey, PA, 17033
JNCI; 68(4):619-622 1982

The specific effects of bile acids as cocarcinogens were investigated. Absorptions of [14C]7,12-dimethylbenz[a]anthracene, [14C]dimethylhydrazine ([14C]DMH), and [3H]inulin from loops of colons from outbred Sprague-Dawley rats and Hartley guinea pigs were determined. In each animal absorption of one carcinogen and inulin was studied in one control loop and in a experimental loop containing either deoxycholic acid (DOC) or chenodeoxycholic acid (CDOC). DOC had a more pronounced effect on increasing loss of carcinogen from the intestinal lumen than did CDOC. This role of bile acids was consistent with their known effect of increasing intestinal permeability. Less carcinogen remained in the colon mucosa when DOC was present in the intestinal lumen. Although [14C]DMH was absorbed more rapidly from the intestinal lumina of guinea pigs than from those of rats, the rat accumulated more of the carcinogen in the intestinal mucosa and liver. (Author abstract) (16 Refs)

41. INHIBITION OF CHEMICAL CARCINOGENESIS BY RETINOIDS.

Moon RC, McCormick DL
Life Sciences Div., IIT Res. Inst., 10 West 35th St., Chicago, IL, 60616
J Am Acad Dermatol; 6(4,part2):809-814 1982

Experiments involving two-stage skin carcinogenesis in mice, the induction of bladder tumors in rats or mice by N-methyl-N-nitrosourea (MNU) or N-butyl-N-(4-hydroxybutyl)nitrosamine (OH-BBN), the induction of mammary tumors in rats by MNU, and the induction of esophageal tumors in rats by N-methyl-N-benzylnitrosamine have demonstrated several important structure-activity relationships in the inhibition of chemical carcinogenesis by retinoids. The aromatic ring, side chain, and polar terminal groups of the retinoid molecule have important effects on the agent's organ distribution and thus its anticarcinogenic activity. Retinoids that significantly inhibit OH-BBN bladder carcinogenesis include 13-cis-retinoic acid (c-RA), ethyl retinamide, 13-cis-ethyl retinamide, 2-hydroxyethyl retinamide, 4-hydroxyphenyl retinamide (4-HPR), 13-cis-4-hydroxyphenyl retinamide, and 2-hydroxypropyl retinamide. Retinoic acid (RA) is a less favorable preventer of MNU-induced mammary tumors in rats than 4-HPR, because 4-HPR accumulates to a lesser extent in the liver and so is less hepatotoxic than RA. Synergistic interactions between retinoids (eg, RA or 4-HPR) and hormonal treatments in MNU mammary carcinogenesis have been discovered. Retinoid treatment from the time of carcinogen administration or the first excision of a carcinogen-induced tumor has greater chemopreventive activity than delayed treatment. The efficacy of delayed retinoid treatment largely depends on the tumor's latent period. The authors' current research involves the identification of new retinoids having lower toxicity and higher chemopreventive activity, combination treatments having synergistic antitumor activity, and the mechanisms of action of the retinoids. (28 Refs)

42. ZINC DEFICIENCY, ALCOHOL, AND A RETINOID: ASSOCIATION WITH ESOPHAGEAL CANCER IN RATS.

Gabrial GN, Schrager TF, Newberne PM
(c/o Newberne) Animal Pathology Lab., Dept. Nutrition and Food Science, Massachusetts Inst. Technology, Cambridge, MA, 02139
JNCI; 68(5):785-789 1982

Groups of Charles River Sprague-Dawley male rats were given intragastric intubations of methylbenzylnitrosamine after receiving one of the following diets for 4 weeks: control, zinc-deficient, or zinc-deficient diet plus 4% ethanol in the drinking water. One zinc-deficient group was zinc repleted after the dosing period; the other group, zinc-deficient plus 4% ethanol, received 13-cis-retinoic acid (13-cis-RA) after the dosing period. Zinc deficiency significantly enhanced esophageal tumor incidence; the addition of ethanol further enhanced tumor incidence. Zinc repletion reduced tumor incidence, whereas the addition of 13-cis-RA enhanced tumor incidence. (Author abstract) (30 Refs)

BIOCHEMICAL, MORPHOLOGICAL AND IMMUNOLOGICAL ASPECTS OF GI CARCINOGENESIS

43. TISSUE POLYPEPTIDE ANTIGEN - A NEW TUMOUR MARKER?

Wagner W, Husemann B, Becker H, Groitl H, Koerfgen HP, Hammerschmidt M
Surgical Clinic, Univ. Erlangen-Nurnberg, 8520 Erlangen, W. Germany
Aust NZ J Surg; 52(1):41-43 1982

The possibility of using Tissue Polypeptide Antigen (TPA) as a tumor marker in the diagnosis and follow-up of patients with malignant tumors was reported. We have taken up these suggestions and examined the possible role of TPA as a tumor marker in gastric and colo-rectal carcinoma. TPA and CEA (Carcinoembryonic Antigen) values were determined in 39 patients with gastric and 60 patients with colo-rectal carcinoma. The tumors were histologically proven. The histological classification of the gastric carcinomas was carried out according to the recommendations of the AJC (American Joint Committee for cancer staging and end results reporting) and that of the colo-rectal carcinomas was according to Dukes. Fifty-two surgical patients with benign diseases were used as controls. In this group the incidence of false positive values was 15.3% for TPA and 23% for CEA. In gastric carcinoma 30 out of 39 patients (76.9%) had on elevated TPA level (medium 275.4 n/l), in contrast CEA was elevated in 18 out of 35 patients (46.1%, medium 24.6 ng/ml). In colo-rectal cancer the TPA level was increased in 61.6% ie 37 out of 60 patients (medium 260.2 n/l). Elevated CEA levels were detected in 38 out of 60 patients (63.6%, medium 192 ng/ml). The mean values of TPA and CEA rise with advancing tumor stages. Elevated TPA levels were also found in non malignant diseases. Possible sources of error are inflammatory reactions. Therefore increased TPA values should be considered indicative of neoplasia only if infections or inflammatory diseases can be excluded and the first value is confirmed by repeated examination. The high incidence of increased values in early tumor stages (Dukes A or AJC 1), seems to justify the inclusion of tests for these antigens into the diagnostic and follow-up routine of gastric and colorectal cancer. (Author abstract) (9 Refs)

44. PATTERNS FOR NORMAL COLON MUCOSA AND COLON ADENOCARCINOMA COMPARED BY TWO-DIMENSIONAL GEL ELECTROPHORESIS.

Tracy RP, Wold LE, Currie RM, Young DS
Section Clinical Chemistry, Mayo Clinic, Rochester, MN, 55905
Clin Chem; 28(4,part2):915-919 1982

A two-dimensional gel 'map' of the proteins in normal cells and transformed cells may well help establish the presence of putative tumor-specific protein antigens, which can be isolated and used as antigens. We so examined normal colon mucosa and colon adenocarcinoma, using a sensitive silver stain. Samples were promptly prepared after excision by rapidly trimming the tissue to a small, grossly homogeneous piece, which was frozen on solid CO2. Frozen histological sections and permanent mounts were also prepared for several areas, to document the cellular constitution and to grade the carcinoma. Sample preparation for electrophoresis is described. The DNA was pelleted by centrifugation (108,000 X g X 1.5 hr). Little or no pellet was observed, indicating complete solubilization. Many of the tumors contained proteases, liberated during sample preparation, so protease inhibitors were included. A highly reproducible pattern was observed for normal mucosa. Comparison of the gels from paired samples with histological data allows many of the spots to be tentatively assigned to the different cell types present in the mucosa (epithelium, connective tissue, or muscularis mucosa) and, in most tumors analyzed, detection of a series of spots that are not detectable in the pattern for normal tissue. These apparently tumor-associated proteins may be of epithelial cell or stromal origin. (Author abstract) (13 Refs)

45. ULTRASTRUCTURAL ALTERATIONS IN THE COLONIC MUCUS LAYER DURING CARCINOGENESIS: A SCANNING ELECTRON MICROSCOPY STUDY.

Traynor OJ, Wood CB, Costa N
Dept. Surgery, Royal Postgraduate Medical Sch., London, England
Adv Exp Med Biol; 144:225-229 1982

Changes in the physical appearance of the colonic mucus layer (CML) during carcinogenesis were examined using scanning electron microscopy. The changes were studied in experimental animals during chemical carcinogenesis and also in humans with colorectal cancer and colonic polyps. The normal CML had a similar appearance in control animals and normal patients. Patients with colorectal carcinoma had advanced changes in the appearance of CML which were similar to those seen in rats with fully developed tumors. In patients with colonic polyps, changes were seen that resembled the preneoplastic appearances in experimental animals. (8 Refs)

46. ULTRASTRUCTURE OF NORMAL ESOPHAGEAL EPITHELIUM AND OF EPITHELIUM IN THE FOCI OF DYSPLASIA.

Kolycheva NI, Fedotovskikh GV, Aleksandrova NM, Zumerov EL
Lab. Tumor Pathomorphology and Geographical Pathology, Kazakh Res. Inst. Oncology and Radiology, Alma-Ata, USSR
Arkh Patol; 44(2):34-41 1982

The results of electron microscope examination of normal esophageal mucosa and esophageal mucosa from the patients with squamous cell carcinoma or adenocarcinoma of the esophagus are reported. Dysplasia of esophageal epithelium was characterized by hyperplasia of the basal cells, nuclear and cellular polymorphism, enlargement of nuclei, and increase of the mitotic activity. Two variants of the esophageal dysplasia were identified. The first variant consisted of dark small spindle-like cells with large nucleus and multiple filaments. The second variant consisted of large clear spherical cells. (16 Refs) (In RUS)

47. HISTOLOGICAL CHANGES IDENTICAL TO THOSE OF CONDYLOMATOUS LESIONS FOUND IN ESOPHAGEAL SQUAMOUS CELL CARCINOMAS.

Syrjanen KJ
Dept. Pathology, Univ. Kuopio, POB 138, SF-70101 Kuopio 10, Finland
Arch Geschwulstforsch; 52(4):283-292 1982

Sixty esophageal specimens obtained from patients subjected to diagnostic endoscopy or surgery for esophageal malignancy were studied to obtain additional information about the supposed role of human papilloma virus (HPV) in human carcinogenesis. The frequencies of the histological parameters suggestive of HPV involvement in the esophageal epithelium associated with squamous cell carcinomas are summarized. The most frequent finding was single cell dyskeratosis, followed by acanthosis, dyskeratotic superficial cells, and multinucleation. (48 Refs)

48. ULTRASTRUCTURAL LOCALIZATION OF CARCINOEMBRYONIC ANTIGEN IN NORMAL INTESTINE AND COLON CANCER. ABNORMAL DISTRIBUTION OF CEA ON THE SURFACES OF COLON CANCER CELLS.

Ahnen DJ, Nakane PK, Brown WR
(c/o Brown), Veterans Admin. Medical Center, 111E, 1055 Clermont St., Denver, CO, 80220
Cancer; 49(10):2077-2090 1982

The distribution of carcinoembryonic antigen (CEA) in normal small intestine, normal colon, and colon cancer of humans was determined immunocytochemically by the peroxidase-labeled antibody method at the light and electron microscopic levels. In the small intestine, CEA was found in protein synthetic organelles, in the mucus, on the microvilli of goblet cells, and on some microvilli of columnar cells adjacent to goblet cells. In the normal colon, CEA was found in protein synthetic organelles of the fully differentiated columnar cells and goblet cells, as well as on the microvilli of the cells. In two well-differentiated colon cancers, the normal preferential surface expression of CEA on the microvilli was maintained, but in six poorly differentiated cancers, CEA was distributed equally over the entire cell surface. We conclude that CEA is a product of goblet cells in the small intestine, columnar and goblet cells in the colon, and colonic cancer cells. CEA on the surfaces of the normal epithelial cells is expressed in a polar manner. This polarity is lacking in undifferentiated neoplastic colon cells, which suggests that failure to establish or maintain the polar expression of normal cell-surface glycoproteins is a characteristic of the neoplastic cells. (Author abstract) (51 Refs)

49. ALTERATIONS IN HUMAN COLONIC MUCIN OCCURRING WITH CELLULAR DIFFERENTIATION AND MALIGNANT TRANSFORMATION.

Boland CR, Montgomery CK, Kim YS
Dept. Medicine, Univ. California, San Francisco, CA, 94121
Proc Natl Acad Sci USA; 79(6,part1):2051-2055 1982

The binding of fluorescein isothiocyanate (FITC)-conjugated lectins to mucin in the human colon was studied by using fluorescence microscopy. In normal mucosa, lectins that preferentially bind to exposed N-acetyl-galactosamine residues (Dolichos biflorus agglutinin and soybean agglutinin) bound selectively to the goblet cell mucin of well-differentiated cells in the upper colonic crypt. By contrast, lectins that require exposed non-reducing galactose residues for binding (Ricinus communis agglutinin I and Bauhinia purpurea agglutinin) preferentially labeled the mucin of less-differentiated goblet cells located in the lower portion of the colonic crypt. The lectin derived from Arachis hypogaea (peanut agglutinin) has a high affinity for a carbohydrate structure not normally exposed in human tissues. This lectin did not label the goblet cell mucin in the normal colon. However, the mucin was labeled in all 21 colon cancer specimens examined. Additionally, the nonmalignant epithelium immediately adjacent to colon cancer (termed 'transitional mucosa') also contained goblet cell mucin that was labeled by FITC-peanut agglutinin. Three conclusions may be drawn from the selective binding characteristics of FITC-lectins to colonic mucins. First, an alteration in the exposed, nonreducing carbohydrate residues occurs in human colonic mucin during the process of goblet cell differentiation. Second, an exposed carbohydrate structure that is not normally present in human tissues is expressed in the mucin produced by malignant colonic epithelium. Third, the presence of the cancer-associated carbohydrate structure in the mucin of transitional mucosa suggests that this tissue may be in the process of early malignant transformation. (Author abstract) (26 Refs)

50. TUMOR MARKERS IN CARCINOMA AND PREMALIGNANT STATES OF THE STOMACH IN HUMANS.

Skinner JM, Whitehead R
Dept. Pathology, Flinders Univ. South Australia, Bedford Park 5042, Australia
Eur J Cancer Clin Oncol; 18(3):227-235 1982

Tissue sections taken from areas of carcinoma, areas of intestinal metaplasia in stomachs bearing carcinoma and areas of intestinal metaplasia in stomachs showing atrophic gastritis only were examined for eight markers: a tumor-derived colon-specific antigen (tCSA), carcinoembryonic antigen (CEA), alphafetoprotein (AFP), pregnancy-specific beta-glycoprotein 1 (SP1), human placental lactogen (HPL), human beta chorionic gonadotrophin (beta-HCG), transferrin (TF) and ferritin (FE). In terms of the number of markers demonstrated in each of the three categories, there is a close similarity between the cells of adenocarcinoma and cells of intestinal metaplasia in cases of cancer, but not to similar metaplastic cells in atrophic gastritis cases. In addition, it appears that the presence of tCSA and SP1 is closely linked to carcinoma, though only approx half of such cases contain these markers. It would also appear that there are two types of morphologically identical intestinal metaplasia, one related to cancer, the other not. No difference was found between so-called intestinal type and diffuse type carcinomas. (Author abstract) (28 Refs)

51. DISTRIBUTION AND RETENTION OF BENZO(A)PYRENE IN RATS AFTER INHALATION.

Mitchell CE
Inhalation Toxicology Res. Inst., Lovelace Biomedical and Environmental Res. Inst., P.O. Box 5890, Albuquerque, NM, 87185
Toxicol Lett; 11(1/2):35-42 1982

The distribution and retention of inhaled radioactive benzo(a)pyrene (BA) was determined in rats. Twenty-four male Fischer-344 rats were exposed for 1 hr to BAP (500 ug/liter air). Tissue, urine, and fecal radioactivity analyses were performed 0, 3, 6, 12, 24, or 48 hr after exposure. Significant amounts of BAP were found in the stomach, small intestine, trachea, lungs, nasal turbinates, larynx, tracheobronchial lymph nodes, kidneys, and liver immediately after exposure. Fifty per cent of the radioactivity cleared from the respiratory tract within 2-3 hr; the remaining cleared between 25 and 56 hr. Fifty per cent clearance of BAP from the liver was obtained in 6 hr. BAP and metabolite concentration in the kidney reached a max value 6 hr after exposure; subsequent clearance was at a constant rate. Radioactivity levels in the spleen, brain, and testes were lower than other major organs, and remained constant for 24 hr after exposure. Radioactivity accumulated rapidly in the cecum and large intestines and subsequently decreased at a constant rate. Excretion of radioactivity was primarily via the feces. Additional studies are necessary to determine the potential mutagenic or carcinogenic risk of BAP exposure in some tissues. (16 Refs)

52. RELATIONSHIP BETWEEN CARCINOGENICITY AND IN VITRO METABOLISM OF NITROSOMETHYLETHYLAMINE, NITROSOMETHYL-N-BUTYLAMINE, AND NITROSOMETHYL(2-PHENYLETHYL)AMINE LABELED WITH DEUTERIUM IN THE METHYL AND ALPHA-METHYLENE POSITIONS.

Farrelly JG, Stewart ML, Saavedra JE, Lijinsky W

Chemical Carcinogenesis Program, NCI-Frederick Cancer Res. Facility, Frederick, MD, 21701

Cancer Res; 42(6):2105-2109 1982

With the use of rat liver preparations, the in vitro microsomal metabolism of methylethylnitrosamine, methyl-n-butylnitrosamine, and methyl(2-phenylethyl)nitrosamine labeled with deuterium in the methyl and alpha-methylene positions has been compared with that of the parent (unlabeled) compounds. All three forms of the liver carcinogen methylethylnitrosamine are metabolized with two sets of kinetic constants. Examination of these kinetic constants suggests that both methylation and ethylation of cellular nucleophiles might be important in the carcinogenic action of these nitrosamines. The esophageal carcinogen, methyl(2-phenylethyl)nitrosamine, gave only one set of kinetic constants during metabolism. The metabolism of the three methylbutylnitrosamines gave results similar to that of the three methylethyl nitrosamines. Except for metabolism of d2-methylbutylnitrosamine to butyraldehyde, two sets of kinetic constants were found. Approximately equivalent amounts of methylating species were produced from d3-methylbutylnitrosamine and d0-methylbutylnitrosamine. (Author abstract) (16 Refs)

53. TOTAL CK ACTIVITY AND ISOENZYME PATTERNS IN NORMAL AND NEOPLASTIC TISSUE OF GASTROINTESTINAL TRACT.

Tsung SH

Dept. Pathology, Methodist Hosp. of Gary Inc., 600 Grant St., Gary, IN, 46402

J Clin Pathol; 35(2):204-206 1982

Total creatine kinase (CK) activity and isoenzyme distribution were determined in normal and tumor tissue of gastrointestinal (GI) tract. Total CK activity per gram wet tissue appeared to be markedly reduced in malignant tumor tissue, yet it was raised in benign tumor tissue. CK-BB was the predominant isoenzyme in both normal and tumor tissue of GI tract. Alteration of isoenzyme pattern was noted between the normal and tumor tissue. In one patient, macro-CK was found in tissue homogenate. (Author abstract) (11 Refs)

PANCREATIC CARCINOGENESIS

54. PATHOLOGY AND PATHOGENESIS OF DISEASES OF THE PANCREAS.

Longnecker DS

Dept. Pathology, Dartmouth Medical Sch., Hanover, NH

Am J Pathol; 107(1):99-121 1982

Pathology and pathogenesis of acute and chronic pancreatitis, carcinoma of the pancreas, cystic fibrosis, and diabetes mellitus are discussed. Islet cell tumors are described, several other less common disorders of the pancreas are listed, and the approaches used in laboratory diagnosis of pancreatic diseases are considered. Pancreatic carcinoma (PC) may arise from duct cells, acinar cells, or islet cells. PC usually involves neoplasms arising in the exocrine pancreas, whereas neoplasms arising in the endocrine pancreas are collectively termed islet cell tumors (ICT). PC is usually diagnosed after local invasion or metastasis has occurred, so that cure by surgical resection is infrequent. The most common histologic type of human PC is a moderately differentiated ductlike adenocarcinoma, which typically incites a desmoplastic reaction. Histologic types of human nonendocrine PC are presented. The incidence of PC rises with age and is greater in males than females (1.6:1 ratio). Epidemiologic studies have demonstrated an increased incidence in individuals with occupational exposure to certain chemicals, and cigarette smoking has been cited as a risk factor for PC. ICT may arise in any of the cell types, and may secrete hormones or may be nonfunctional. Hormone secretion by a tumor may cause a clinical syndrome reflecting the effect of excess hormone. Some nonfunctional ICT are malignant, and their clinical impact results from common duct obstruction or invasion and metastasis. ICT may be present with other endocrine tumors in the multiple endocrine neoplasia I syndrome. (44 Refs)

55. EFFECTS OF LOW-DOSE RADIATION. A CORRELATION STUDY.

Edling C, Comba P, Axelson O, Flodin U

(c/o Axelson) Dept. Occupational Medicine, Univ. Hosp., S-581 85 Linkoping, Sweden

Scand J Work Environ Health; 8(Suppl1):59-64 1982

Based on information in the literature, five types of malignancies (lung, breast, and pancreatic cancer, leukemia, and multiple myeloma) probably respondent to irradiation induction and therefore likely to correlate with background radiation were chosen for the correlation study on effects of low-dose radiation. Mortality rates age-standardized directly for lung and breast cancer and leukemia during 1969-1978 and for pancreatic cancer and multiple myeloma during 1961-1973 in the counties of Sweden and for persons 40 yr old and over, along with estimates of background radiation (cosmic radiation excluded), Pearson coefficients and p-values are presented. Significant correlation was observed between the estimates of background radiation and lung cancer, for both males and females. A similar correlation was observed for pancreatic cancer in both sexes. Leukemia showed a correlation of borderline significance for males and a weaker correlation for females. Breast cancer (in women only) and multiple myeloma did not show any significant correlation. Risk estimates for lung cancer per working level mo (WLM) and per 10(6) person-yr for persons greater than 50 yr old in various Swedish populations (including Zn-Pb miners) and estimates given in a previous report indicate that 25-35 cases per 10(6) person-yr and per WLM might result from radon daughter exposure. (31 Refs)

56. INFLUENCE OF AGE, SEX AND CANCER ON THE ACTIVITIES OF GAMMA-GLUTAMYL TRANSPEPTIDASE AND OF DIPEPTIDYL AMINOPEPTIDASE IV IN RAT TISSUES.

Fujiwara K, Katyal SL, Lombardi B

Faculty Pharmaceutical Sciences, Nagasaki Univ., Bunkyo-machi 1-14, Nagasaki 852, Japan

Enzyme; 27(2):114-118 1982

Gamma-glutamyl transpeptidase (GTP; EC 2.3.2.2) is an enzyme known to show activity changes during development and carcinogenesis. Its activity was measured in the livers and lungs of female and male rats of different ages, in Morris hepatomas and in experimentally induced pancreatic carcinomas. For comparison purposes, the activity of another peptidase, dipeptidyl aminopeptidase IV (DPAP; EC 3.4.14.1), was assayed in the same tissues. GTP activity was high in fetal liver and hepatomas, but low in adult rat liver, with a marked sex difference, 3x higher in the female than in the male. In the pancreas, however, the activity of the enzyme was high in the adult but low in the fetus and in pancreatic carcinoma. There were no marked developmental changes or sex differences in pulmonary GTP activities. DPAP levels were low in fetal and neonatal liver and lung, they increased rapidly after birth and showed no sex differences in the adult. In Morris hepatomas and in pancreatic tumors the activity of DPAP was significantly lower than in normal adult liver and pancreas. These results suggest that measurements of GTP (and, to a lesser extent, DPAP) are remarkably suitable for the study of neoplastic cells and tissues. (Author abstract) (19 Refs)

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57. ESTROGEN RECEPTORS IN 7,12-DIMETHYLBENZ(A)ANTHRACENE (DMBA) INDUCED PANCREATIC CARCINOMA IN RATS AND IN HUMAN PANCREATIC CARCINOMA.

Satake K, Yoshimoto T, Mukai R, Umeyama K
First Dept. Surgery, Osaka City Univ. Medical Sch., Asahi-Machi, Abeno-Ku, Osaka 545, Japan
Clin Oncol; 8(1):49-54 1982

DMBA-induced pancreatic carcinoma in rats and human pancreatic carcinoma have been assayed for estrogen receptors. Estrogen receptors were detected in 43.7% of DMBA-induced pancreatic carcinoma and in one of seven human pancreatic carcinomas. Histologically, the tumors were ductal-type adenocarcinoma. The results suggest that changes of estrogen receptor levels may have an important role in developing pancreatic carcinoma, and it is concluded that the detection of estrogen receptors will become an important method for the investigation of pancreatic carcinoma in the near future. (Author abstract) (16 Refs)

REVIEWS AND OTHER RELATED STUDIES

58. LARGE BOWEL CANCER: THE NEXT MOVE?

Hughes ES, McDermott FT, Polglase AL, Johnson WR, Pihl EA
Dept. Surgery, Monash Univ., Alfred Hosp., Commercial Road, Prahran, Victoria 3181, Australia
Med J Aust; 1(1):36-37 1982

Despite a an intensive anti-cancer campaign and a shorter delay between the appearance of symptoms and consultation with a physician, the survival rates for large bowel cancer (LBC) have not improved significantly. In some studies, results have actually worsenned. Prophylaxis of LBC requires the detection of people who are more likely to develop carcinoma of the large bowel. A tendency for certain families to be affected by the disease has been observed although no predictable pattern has been discerned. Patients who have had a LBC successfully removed are at greater risk of developing a second new primary tumor. Benign tumors are very common in the human colon. Diagnosis and treatment of such polyps are described. Untreated, familial polyposis of the large bowel develops into malignancy. The incidence of LBC is much higher in patients with ulcerative colitis than in the general community. Factors possibly related to LBC, such as low residue diet, high beef (particularly fried) diet, water chlorination particularly in areas deficient in selenium, occupational hazards, and other environmental factors, must be determined and eliminated. (16 Refs)

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NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. TOXICITY AND METABOLISM OF ACRYLONITRILE.
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Zaklad Metabolizmu Substancji Toksycznych, Instytut Medycyny Pracy, ul. Teresy 8, 90-950 Lodz, Poland
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Dept. Biological Sciences, Portsmouth Polytechnic, King Henry I St., Portsmouth, PO1 2DY, Hants, England
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3. CARCINOGENICITY OF AIRBORNE FINE PARTICULATE BENZO(A)PYRENE: AN APPRAISAL OF THE EVIDENCE AND THE NEED FOR CONTROL.
Perera F
Natl. Resources Defense Council, Inc., 122 East 42nd St., New York, NY, 10168
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10. NEPTUNIUM - THE NEGLECTED ACTINIDE: A REVIEW OF THE BIOLOGICAL AND ENVIRONMENTAL LITERATURE.
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PREVALENCE OF GI CANCER IN HUMAN POPULATIONS

1. HEREDITARY COLONIC ADENOCARCINOMA (HCA): AN AUTOSOMAL DOMINANT CONDITION WITH ADULT ONSET (MEETING ABSTRACT)

McCormack MK, McCormack PC
CMDNJ-Rutgers Medical School, Piscataway, NJ
Am J Hum Gen; 33(6):66A 1982

Inherited forms of colon cancer without polyposis account for as much as 25% of all large bowel cancers while inherited polyposis represent only 1% or less. At least four distinct types of hereditary non-polyposis colonic cancers have been identified: HCA with colonic and occassionally stomach; Hereditary gastrocolonic cancer, with adenocarcinoma of the colon and stomach and Torre's or Muir's Syndrome with multiple sebaceous tumors, adenocarcinoma of the small intestine, stomach, uterus, colon, transitional cell cancer of the ureter and bladder and squamous cell carcinoma of larynx, esophagus and vulva. Three unrelated, independently ascertained kindreds with three generations of affected individuals (11 females and 6 males) with HCA were identified. In all cases affected individuals

HE 20.3173/2:

showed only evidence of a primary colonic adenocarcinoma, however two affected individuals demonstrated also basal cell carcinoma and gastric cancer respectively. Many of the affected individuals demonstrated multiple primary tumors. The age of onset was generally earlier than that observed for the nonfamilial colon cancer and involved the more proximal colon. In only one case was the age of onset greater than 70 years. The remainder of the cases had an age of onset between 28 and 53 years. In all three kindreds the mode of inheritance was autosomal dominant. Chromosome studies of probands were within normal limits. (no Refs)

2. TRENDS IN THE INCIDENCE OF GASTRIC CARCINOMA (MEETING ABSTRACT)

Nobrega FT
Preventive and Internal Medicine, Mayo Clinic, Rochester, MN
Eleventh Annual William Beaumont Gastrointestinal Symposium, March 24-26, 1982, El Paso, Texas. William Beaumont Army Medical Center 56 pp., 1982.

During the past 50 years or more a dramatic decline in the mortality from gastric carcinoma has been observed in virtually every country in the world including the United States. Some investigators suspect that this decline is due to refinements in the diagnosis and classification of abdominal malignancies rather than a true decline in the incidence of gastric cancer. Since the high quality of medical care and the record system in Rochester, Minnesota assures the identification of virtually every patient in the local population with a serious illness, it seemed appropriate to study the incidence and long-term trends of gastric cancer in this community. Furthermore, a study in Rochester has the advantage that clinically diagnosed as well as tissue confirmed cases throughout the period from 1935 through 1979 could be readily studied. Also it was feasible to retrieve the tissue slides of nearly every diagnosed case for review by a surgical pathologist. Trend analysis reveals a consistent decline in the incidence of gastric carcinoma whether death certificates, as the sole source of cases, are included or excluded. The analysis of either all clinically confirmed, or only tissue confirmed, cases reveals a statistically significant decrease in stomach carcinoma throughout the study period. Of additional interest these declines continue to be observed even if only the more recent time periods (1955-79) are examined. The reason for this finding remains obscure but the study suggests that improvements in diagnostic accuracy alone cannot account for this remarkable downward trend in gastric malignancy. (no Refs)

3. GENETICS OF A FAMILIAL CANCER SYNDROME CHARACTERIZED BY SARCOMAS AND DIVERSE NEOPLASMS (MEETING ABSTRACT)

Blattner WA, Zener KA, Greene MH, Mulvihill JJ, Li FP, Fraumeni JF
National Cancer Institute, Bethesda, MD, 20205
Proc Am Soc Clin Oncol; 1:C-711 1982

In 1969, Li and Fraumeni described a familial syndrome of sarcomas (S), breast (B), and other neoplasms affecting children and young adults. The current survey of 26 families with S and one other cancer (Ca) (excluding non-melanotic skin) in first-degree relatives was undertaken to characterize the syndrome. Among 1,242 family members, 283 primary Ca's were ascertained. In 27 cases multiple primary Ca's were documented including 1 with 4 separate primaries and 3 with triple primary Ca's. Excluding the 26 S in index cases, the distribution of Ca types was: B 21%, S 12.8%, lung (Lu) 9.3%, brain (Br) 8.1%, leukemia (L) 6.6%, gastric 4.2% and pancreas 3.9%. Adrenal cortical cancers were reported in 3 children. The age distribution for certain neoplasms (S, L, Br) resembled the expected pattern, while others (B, Lu) tended to occur at a younger age than usual. Review of pedigrees revealed 2 patterns: in 12 families, Ca's clustered in distant branches traced through a single line of descent; in 10, Ca's clustered in a single sibship with multiple ancestral branches contributing to the familial tumor diathesis. Demographic characteristics and tumor types were indistinguishable in the 2 groups. These data support the concept that susceptibility mechanisms are shared by several forms of Ca including bony and soft-tissue sarcomas; brain, breast, and lung tumors; and leukemia. (1 Ref)

4. EPIDEMIOLOGY OF STOMACH CANCER IN SAN MARINO AND IN EMILIA-ROMAGNA.

Baldi E, Salerno Mele P, D'Imperio N, Mularoni E
Istituto di Patologia Medica e Medicina del Lavoro, Universita di Bologna, Bologna, Italy
G Clin Med; 62(11):782-788 1981

Statistics of incidence of gastric cancer (GC) in the population of Republic of San Marino (SM) and in the Italian region of Emilia-Romagna (ER) were compared. Endoscopic examinations were performed in 1,000 patients in SM and in 10,000 in ER. In SM 40 of the patients (23 men, 17 women) had GC and in ER an incidence of 4% and 2.37%, respectively, was found in 237 patients. (15 Refs) (In ITA)

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN GI CARCINOGENESIS

5. POSSIBLE ETIOLOGICAL FACTORS IN THE DEVELOPMENT OF ESOPHAGEAL CANCER.

Horvath O, Csikos M, Petri I, Petri A, Szontagh E, Imre J
I. Sebeszeti Klinika, Szegedi Orvostudomanyi Egyetem, Szeged, Hungary
Orv Hetil; 123(16):971-976 1982

Possible etiological factors of esophageal carcinoma were studied in 385 patients. Regular alcohol consumption was determined in 56.4% of all patients. The corresponding percentage was 70% in another group of 100 patients with esophageal carcinoma, and the daily alcohol consumption of 35/100 patients exceeded 150 g. Past gastric resections were performed in 20/385 patients. The av interval between resection and the manifestation of esophageal carcinoma was 14 yr. Achalasia lasting 15-21 yr before the development of esophageal carcinoma was diagnosed in 5 patients. Stricture of the esophagus was present in 34/385 cases. Severe respiratory tract infections were found in the anamnestic data of nearly two thirds of all patients, pulmonary tuberculosis in 16/385. Eight-one of the 100 patients of the second group were found to be smokers. Second tumors were found in 11/385 patients. They included sublingual gingival and laryngeal tumors in two patients each, gastric tumors in three, prostate and renal tumors in one each. Undernutrition, vitamin deficit, reflux esophagitis and inadequate oral hygiene are also possible etiological factors of esophageal carcinoma. (56 Refs) (In HUN)

6. SMOKING AND CANCER.

Lapis K
No affiliation given
Magy Tud; 89(2):119-127 1982

Epidemiological and etiological relationships between smoking and cancer, especially lung caner, are discussed. The carcinogenic substances occurring in tobacco and cigarette smoke include polycyclic aromatic hydrocarbons, such as benzo(a)pyrene, N-nitrosamines, such as N-nitrosonornicotine, and 210-polonium. Increased incidence of cancer of the larynx, pharynx, lips, oral cavity, tongue, esophagus, urinary bladder, pancreas, and especially lung was observed among smokers compared with nonsmokers. (no Refs) (In HUN)

7. STUDIES OF THE MORTALITY OF A BOMB SURVIVORS. 7. MORTALITY, 1950-1978: PART I. CANCER MORTALITY.

Kato H, Schull WJ
Radiation Effects Res. Foundation, Hiroshima, Japan
Radiat Res; 90(2):395-432 1982

Mortality of survivors of the atomic bombing of the cities of Hiroshima and Nagasaki during World War II is updated to include the years 1975-1978. The excess in leukemia deaths continued to decrease during these yr from the peak in 1950-1954, and in 1975-1978 an increased mortality with dose was observed only in Hiroshima. Cancers other than leukemia have increased yearly from about 1960 and, averaged over all periods, the risk of these cancers now equals (Nagasaki) or exceeds (Hiroshima) that of leukemia. The risks of lung, breast, and stomach cancers, which were shown be significantly increased in the yr 1950-1974, have continued to rise in 1975-1978, but there has been no apparent additional increase in risk in 1975-1978 for esophageal or urinary tract cancers, which had increased previously. An elevated risk of colon cancer has become newly evident. The significant increase with dose observed for malignant lymphoma in the previous report appeared in retrospect to be spurious, stemming possibly from the inclusion of multiple myeloma. No increased risk of uterine cancer has been seen. A greater excess of a variety of tumors was observed in Hiroshima than in Nagasaki in all periods combined. The significance of the relationship between radiation and cancer is discussed. (17 Refs)

8. A HISTORICAL PROSPECTIVE MORTALITY STUDY OF WORKERS IN COPPER AND ZINC REFINERIES.

Logue JN, Koontz MD, Hattwick MA
Epidemiologic Studies Branch (HFX-130), Div. Biological Effects, Bureau of Radiological Health, United States Food and Drug Admin., Rockville, MD, 20857
JOM; 24(5):398-408 1982

Earlier health studies of workers in electrolytic refinery operations have raised concern that workers may experience excess morbidity and premature death as a result of hazardous occupational exposures. This study was designed to determine if the refinery operation is associated with any excess mortality patterns. A cohort of 4,802 male workers exposed for at least 1 year during 1946-1975 was assembled from nine US zinc and copper refineries. Vital status was ascertained for 4,241 (88%) of the cohort. Death certificates were obtained for 84% (355/423) of the deceased. Overall standard mortality ratios (SMRs) were calculated to be 92 for the cohort, 97 for the subgroup of copper refinery workers, and 83 for the subgroup of zinc refinery workers. Significantly high cause-specific SMRs were as follows: (1) cerebrovascular disease (CBVD) for the cohort; (2) all cancers, cancer of the digestive tract, and CBVD for the copper subgroup; (3) all cancers, cancer of the respiratory tract, and CBVD for one plant for demonstrated a significantly high overall SMR (133). The significant excess of cancer deaths among the study cohort is largely due to the plant that exhibited the significantly high overall mortality rate, but lack of smoking data qualifies this finding. The significant excess of CBVD seems to be consistent across plants and further research seems warranted to verify the finding. (Author abstract) (32 Refs)

9. THE ASSOCIATION OF OCCUPATION AND INDUSTRY WITH MORTALITY IN RHODE ISLAND (1968-1972).

Gute DM
Rhode Island Deot. Health, Providence, RI
The Association of Occupation and Industry with Mortality in Rhode Island (1968-1972). Available from National Technical Information Service, Springfield, VA, as HRP-0903529/6c, 144 pp., 1981.

In recognition of the importance of occupational health as a problem area, this study was undertaken to begin to target in as effective a manner as possible, scarce occupational health resources. The analysis attempts to identify occupations and industries which may place workers at increased risk of specific causes of death. Data was obtained from the records of approximately 43,000 Rhode Island decedents during the years 1968-1972. The results of the Rhode Island study are reported by sex, age occupation group, industrial group, and cause of death. The study found, for males, an increased risk of chronic obstructive lung disease among textile workers, an excess of accidental death among construction workers and an increase in lung cancer for construction craftsmen, transport operatives, cleaning service workers, and metal craftsmen. For females, the finding of particular interest is the risk of stomach cancer among workers in the jewelry industry. Further study and analytic research should be performed in these areas. Several historic occupation mortality studies are reviewed and the different methodologies used in these studies are described. Tables and figures are used to present the data. References are included at the end of each chapter. The appendices contain related data. (Author abstract)

10. CANCER-ENVIRONMENT REGISTRY DATA INSUFFICIENT FOR ANALYSIS OF POSSIBLE RELATIONSHIP BETWEEN PARENT'S OCCUPATION AND TUMORS IN THEIR CHILDREN.

Berglund K, Iselius L, Lambert B, Lindsten J, Ludvigsson J, Stjernfeldt M
Statens miljomedicinska laboratorium, Stockholm, Sweden
Lakartidningen; 79(15):1484-1487 1982

Data in the cancer-environment registry were analyzed to identify the cancer frequency in different occupational groups. It was not possible to analyze the frequency of malignant diseases among children as a function of their parent's occupation due to lack of appropriate data in the cancer registry. The standardized morbidity rates (SMR) in men were found to be increased after mass significance analysis for cancer of the lips, tongue, salivary glands, floor of mouth and larynx in workers (rubber industry); for cancer of the esophagus and gastrointestinal tract in engineers and technicians exposed to chemicals; for cancer of the biliary tract, liver and pancreas in bookkeepers, cashiers, motor vehicle operators, barbers and beauticians; for cancer of the nose, paranasal sinuses, middle ear, trachea, bronchi, lungs and pleura in chemists, pharmacists, bookkeepers, cashiers, gasoline station attendants, motor vehicle operators, painters, printers, workers (rubber industry), barbers and beauticians; for cancer of the kidneys and urinary tract in engineers and technicians exposed to chemicals, bookkeepers, cashiers, typists, workers (rubber and leather industries), barbers and beauticians; for cancer of skin (including melanoma) in bookkeepers, cashiers, bank employees and workers (leather industry). In women the SMR were increased for cancer of the esophagus and gastrointestinal tract among bookkeepers, cashiers and bank employees; for cancer of the kidneys and urinary tract among secretaries, stenographers, typists and pharmacists, and for cancer of the skin (including melanoma) among secretaries, stenographers and typists. (15 Refs) (In SWE)

DIETARY AND DIGESTIVE FACTORS IN GI CARCINOGENESIS

11. FUSARIUM MYCOTOXINS AND THE EFFECTS OF HIGH-FAT DIETS.

Schoental R
Dept. Pathology, Royal Veterinary Coll., Univ. London, Royal College St., London NW1 0TU, England
Nutr Cancer; 3(2):57-62 1981

Some of the inconsistencies encountered in epidemiological and experimental studies on the role of various types of fats in the etiology of cardiovascular disorders and certain tumors (of the breast, endometrium, and colon, among others) may be related to the presence of adventitious contaminants in the fats. Among the contaminants, mycotoxins, especially those produced in agricultural products by the Fusarium field-microfungi (the irritant trichothecenes, the estrogenic zearalenone, and other resorcylic acid lactones), warrant particular attention. Their production is favored by the wet, cool weather prevailing in areas notable for high incidences of the aforementioned disorders. The recent development of sensitive radioimmunoassays for the detection and estimation of some of these mycotoxins should facilitate the testing of the above hypothesis. (Author abstract) (39 Refs)

12. NITROSAMINES.

Aigner K
Pneumonologische Abteilung, Krankenhaus der Elisabethinen, Fadingerstr. 1, A-4020 Linz-Donau, Austria
Wien Med Wochenschr; 132(71,Suppl):75-79 1982

Health hazards of nitrosamines (NA) are reviewed. NA are formed by the reaction of amines or amides with nitrite or nitrous gases. NA are found in foods, cosmetics, technical oils, pesticides, tobacco, and drugs. Elevated levels of NA have been found in patients with some diseases, including gastric carcinoma. Animal studies have confirmed the carcinogenicity of NA. Further research is required to reduce intake and formation of NA in humans. (17 Refs) (In GER)

13. ALCOHOL: THE MYSTERIES OF THE WEST.

Chailleux JP
No affiliation given
Vivre; (234):15-18 1982

The incidence of digestive tract cancer, particularly esophageal cancer, shows a high correlation with alcohol and cigarette consumption. In regions of France where alcohol consumption is high, (Brittany and Normandy) the cancer mortality rate for digestive tract cancer is elevated. Causes of the correlation between alcohol intake and cancer development are discussed. (4 Refs) (In FRE)

14. EFFECT OF DIETARY FIBRE COMPONENTS (CELLULOSE AND LIGNIN) ON EXPERIMENTAL COLON NEOPLASIA (MEETING ABSTRACT)

Sloan DA, Fleiszer DM, Murray D, Brown RA
McGill University Surgical Clinic, Montreal General Hospital, Montreal, Quebec, Canada
Joint Meeting of the Society of Surgical Oncology and Society of Head and Neck Surgeons, April 18-23, 1982, Marco Island, Florida. The Society of Surgical Oncology and the Society of Head and Neck Surgeons 265 pp., 1982.

Considerable interest has been focused on the role of dietary fiber in the etiology of colon cancer, both from epidemiologic and experimental perspectives. Using the well established 1,2-dimethylhydrazine model, we examined the effects of the two major crude fiber components on experimental colon neoplasia. Sixty Sprague-Dawley weanling rats were divided into three dietary groups and pair fed one of three separate but nutritionally identical diets: 'low fiber' (3.8% crude fiber) 'high fiber, cellulose' and 'high fiber, lignin' (both 28.7% crude fiber). The animals were treated with weekly subcutaneous 1,2-dimethylhydrazine injections for twenty weeks at a dose of 20 mgm per kg, and sacrificed at weeks twenty-nine and thirty of the experiment. Both cellulose and lignin fed animals experienced a stool bulking effect with greater 48 hour stool weight than low fiber animals. Animals fed the low fiber diet had significantly longer transit times than the high fiber fed animals. The necropsy results show that only the cellulose (and not the lignin) group had significantly fewer animals with tumor when compared to the low fiber group. The experiment suggests that while cellulose and lignin fibers both have similar stool bulking effects, only cellulose shows a protective effect against the induction of experimental colon cancer. (no Refs)

15. DIETARY HABITS AND COLONIC CARCINOMA.

Bloch R
Klinik fur Verdauungs- und Stoffwechselkrankheiten, Am Weinberg 3-5, D-6430 Bad Hersfeld, W. Germany
Hepatogastroenterology; 28(5):231-232 1981

Dietary factors related to a high incidence of colon cancer (CC) in industrialized countries of Europe and in the United States are discussed; such factors include excesses of fat, protein, meat, and total calories, and deficiencies of fiber, vitamins A, C, and E, and selenium. The ratio of fat to crude fiber has been shown to be more important than the absolute intake of fats and fiber in development of CC. Alcohol, tobacco, appetite-depressing drugs, and laxatives have not been shown to be causative agents in CC. (13 Refs)

16. METABOLISM OF 2,4-DINITROTOLUENE BY RAT HEPATIC MICROSOMES AND CECAL FLORA.

Dent JG, Schnell SR, Guest D
Chemical Industry Inst. Toxicology, Res. Triangle Park, NC, 27709
Adv Exp Med Biol; 136(partA):431-436 1982

The metabolism of 2,4-dinitrotoluene (2,4-DNT) in hepatic microsomes and in the intestinal flora was investigated. Hepatic microsomes were obtained by preparation of livers from male Fischer 344 rats. Cecal microflora was obtained from male rats. [U-14C] 2,4-DNT was incubated at 100 uM with microsomes in 66 milliMoles tris HCl (pH 7.4) for 1 hr; a NADPH generating system was included. An oxygen scavengering system was included in the incubations with nitrogen. The patterns of metabolites produced by the hepatic microsomes was dependent on the oxygen tensions in the incubations. In contrast to microsomes, cecal microflora did not metabolize 2,4-DNT in an air atmosphere, but the 2,4-DNT was rapidly reduced in anaerobic conditions. Both 2-and 4-nitroso-nitrotoluenes were detected in the cecal flora incubations. Comparison of the metabolism of the DNT by the cecal contents and the hepatic microsomes indicated that the reductive metabolic capacity of the cecal contents on a per g wet wt basis exceeds that of the liver by a factor of 1,000, suggesting that the cecum represents a major site for reductive metabolism of DNT; the 2,4-DNT undergoes reduction at either the 2 or 4 nitro group to a nitroso-nitrotoluene. Reduced metabolites of DNT absorbed from the gut would be substrates for the mixed function oxidase (MFO) enzymes in the liver. Oxidations by the MFO system would lead to highly reactive intermediates in the liver. Thus, the liver and cecal microflora acting in concert may be responsible for the carcinogenic activity of DNT. (7 Refs)

OTHER ETIOLOGIC FACTORS IN GI CARCINOGENESIS

17. PRECANCEROUS LESIONS OF THE UPPER DIGESTIVE TRACT.

Mittelmeier HO, Pliess G

Pathologisches Institut der Stadt Nurnberg, Flurstrasse 17, D-8500 Nurnberg 90, W. Germany

Therapiewoche; 32(14):1871-1872,1874,1876,1878,1883 1982

Various lesions of the upper digestive tract, termed precancerous lesions (PL), carry an increased risk of malignant growth. PL arise in particular locations. Risk factors contribute to the development of PL. PL develop as epithelial preneoplasias, which then become carcinoma in situ or early carcinoma; conversion to invasive carcinoma and then to metastatic carcinoma may follow. Risk factors for carcinoma of the esophagus include use of alcohol and tobacco; risk lesions include benign strictures, old alkali burns, pulsion diverticula, achalasia, and hyperkeratosis with Plummer-Vinson syndrome. PL of the esophagus include hyperkeratosis with tylosis palmaris et plantaris and columnar epithelial metaplasia associated with reflux esophagitis. Risk factors for carcinoma of the stomach include familial history of stomach cancer, blood type A, and acanthosis nigricans; risk lesions include stomach resection, gastric polyps, Menetrier's disease, pernicious gastritis, and lymphatic hyperplasia. PL of the stomach include adenomatous polyps, border-line lesions of the protruded type, and polypous early carcinoma of Types I and IIa. Carcinomas of the duodenum are very rare. Risk factors are unknown; risk lesions include gluten enteropathy, herpetiform dermatitis, and hereditary intestinal polyposis associated with Peutz-Jeghers syndrome or Gardner's syndrome. PL of the duodenum are unknown. High-risk lesions of the upper digestive tract are indications for endoscopic biopsy at appropriate intervals. (5 Refs) (In GER)

INDUCTION OF GI CARCINOGENESIS IN ANIMALS

18. MORPHOLOGIC ANALOGY OF INTESTINAL TRACT CARCINOGENESIS IN ADENOMATOUS POLYPOSIS AND THE AZOXYMETHANE-TREATED RAT MODEL (MEETING ABSTRACT)

Hamilton SR, Stephens RB, Natuzzi E, Boitnott JK, Yardley JH

Department of Pathology, The Johns Hopkins University School of Medicine and Hospital, Baltimore, MD

71st Annual Meeting of the International Academy of Pathology (United States-Canadian Division), March 1-5, 1982, Boston, Massachusetts. International Academy of Pathology 95 pp., 1982.

Parenteral administration to rodents of azoxymethane (AOM), a metabolite of dimethylhydrazine, provides a widely used model of colonic carcinogenesis. Unlike usual large bowel carcinoma in human beings (ULBC) but analogous to adenomatous polyposis (AP), the AOM model has a high incidence of multiple colonic carcinomas and proximal small bowel carcinomas, particularly with higher dosage of carcinogen. In this study, grossly normal colonic mucosa from 10 resections for ULBC, six prophylactic colectomies for AP, four AOM-treated, and four control rats was examined for dysplastic crypts in en face histologic sections oriented in the plane of the luminal surface. AOM-treated rats were male Fischer 344 rats given 10 weekly subcutaneous injections of 7 mg of AOM per kg, starting at 11 weeks of age and killed 24 weeks after the first dose. Grossly normal colonic mucosa showed 0.03 foci of dysplastic crypts per sq cm examined in ULBC, 3.0 in AP, 2.9 in AOM rats, and 0.05 in controls rats. Dysplastic crypts composed 0.005 per 1000 crypts examined from right colon in ULBC, 39 in AP, and 0.3 in AOM rats, intermediate to AP and ULBC. Grossly normal proximal small bowel mucosa in the AOM rats showed 1.1 dysplastic foci per sq cm. (no Refs)

19. CARCINOGENICITY OF FLUOROCARBONS: ASSESSMENT BY SHORT-TERM IN VITRO TESTS AND CHRONIC EXPOSURE IN RATS (MEETING ABSTRACT)

Longstaff E, Robinson M, Bradbrook C, Styles JA, Purchase IF

Central Toxicology Laboratory, Alderley Park, N. Macclesfield, Cheshire, England

Toxicologist; 2(1):106 1982

Twenty-one fluorocarbons were evaluated for mutagenic activity using Salmonella typhimurium. Twelve of these were also assessed in the BHK21 cell transformation assay. Monochlorodifluoromethane (FC-22), chlorofluoromethane (FC-31), 1-chloro-1,1-difluoroethane (FC-142b), 1,1-difluoro-2-chloroethane (FC-142) and 1,1,1-trifluoroethane (FC-143a), showed mutagenic activity towards Salmonella and FC-31 and FC-142b were positive in the BHK21 test. The in vivo carcinogenicity of some of these chemicals was also assessed by a long-term bioassay. Wistar rats (40/sex/group) were dosed by gavage with 300 mg/kg bodyweight of 3% w/v in corn oil FC-22, FC-31, FC-133a (2-chloro-1,1,1-trifluoroethane), FC-134a (1,1,1,2-tetrafluoroethane) and FC-143a, five days a week for one year. One undosed and two dosed control groups were employed. The study was terminated at 126 wks. Rats dosed with FC-31 showed a high incidence of stomach squamous cell carcinomas and fibrosarcomas. Female rats dosed with FC-133a had a markedly increased incidence of uterine adenocarcinomas while the males of the group had a greatly increased incidence of testicular interstitial cell tumors and all had marked testicular atrophy. Carcinogenicity was not seen with any of the other fluorocarbons. (no Refs)

20. COLONIC LYMPHOID TISSUE AND ITS INFLUENCE ON TUMOUR INDUCTION IN DIMETHYLHYDRAZINE-TREATED RATS (MEETING ABSTRACT)

Bland PW, Britton DC
Department of Clinical Investigation, Royal United Hospital, Bath, England
Br J Cancer; 44(2):275 1981

The mucosa of the large intestine contains a large amount of organized lymphoid tissue, but little is known of its contribution to antigen-processing, secretory immunity or tumor immunity. In the rat, mucosal lymphoid follicles are grouped together into discrete colonic lymphoid patches (CLP) in the proximal, mid and terminal colon. We have investigated the relationship between CLP and colonic neoplasia in the rat model of 1,2-dimethyl-hydrazine (DMH)-induced colonic adenomas and adenocarcinomas. One hundred male, 7-week old Sprague-Dawley rats were injected sc with DMH (21 mg/kg) weekly for 20 weeks and groups were autopsied from weeks 20-40. Fifty-two rats bore a total of 71 colonic tumors. Fifty-seven (80%) of these tumors (adenomatous polyps and both polypoid and sessile adenocarcinomas) arose from the epithelium overlying CLP, and many of the remainder were closely associated with isolated follicles. Light and electron microscopy of CLP in control rats showed that constituent follicles were separated from the gut lumen by a flattened lymphoepithelium, highly specialized to facilitate antigen transport. Adjacent follicles were separated by groups of crypts generating normal columnar epithelium. The contribution of tumor induction in these interfollicular crypts from altered epithelial-cell kinetics and interaction with the underlying lymphoid elements, is currently under investigation. (no Refs)

21. INDUCTION OF SQUAMOUS CELL CARCINOMA IN THE FORESTOMACH OF F344 RATS TREATED WITH BUTYLATED HYDROXYANISOLE.

Ito N, Hagiwara A, Shibata M, Ogiso T, Fukushima S
First Dept. Pathology, Nagoya City Univ. Medical Sch., 1 Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya 467, Japan
Gan; 73(2):332-334 1982

Carcinogenic effects of butylated hydroxyanisole (BHA) were studied in 4-wk-old F344 rats. The BHA was incorporated into Charles River basal diets as pellets at 2% and 0.5% concentrations and fed to two groups of 50-52 rats each. Control groups of 51 rats of each sex were given control diet. After wk 104 on the diet, all animals were fed control basal diet until wk 112. Animals were sacrificed and examined grossly and histologically. There was a significant increase in mortality of females at wk 72 and males at wk 80 in all groups of rats. At autopsy, tumors were found in the forestomach of both sexes of rats fed the BHA diet. Gross examination of the tumors showed that they were papillary and infiltrated into the muscle and serosal layers of the forestomach. Tumors were greyish-white warty or villous nodules, and areas of ulceration were observed in some animals. Metastasis to the omentum or liver were observed in one rat each. Histologically, marked proliferation of basal cells and keratin forming elements were observed in the papillomas. Well-differentiated and poorly-differentiated types of squamous cell carcinoma were observed. The well-differentiated type had more keratinization and the cancer cells had many mitotic figures and atypism. Tumors were also found in the liver, pancreas, lungs, ovary, testes, and pituitary gland in some of the rats, but incidences of these tumors were similar between the control and experimental rats. The results showed that BHA, administered po in the diet, is carcinogenic in F344 rats and primarily affects the forestomach. (6 Refs)

22. INDUCTION AND CHARACTERIZATION OF GASTRO-DUODENAL LESIONS IN MICE GIVEN CONTINUOUS ORAL ADMINISTRATION OF HYDROGEN PEROXIDE.

Ito A, Naito M, Naito Y, Watanabe H
Dept. Cancer Res., Res. Inst. Nuclear Medicine and Biology, Hiroshima Univ., Kasumi 1-2-3, Minami-ku, Hiroshima 734, Japan
Gan; 73(2):315-322 1982

The tumorigenicity of hydrogen peroxide (HP) was examined by administering 0.4% HP solution in drinking water to various strains of mice. In C57BL mice, gastric lesions in the forestomach occurred in over 67% of the mice treated with HP for 120 days and duodenal lesions were noted in over 80% of the mice that received HP for 60 days. Gastric lesions were found only in the glandular stomach and duodenal lesions were restricted to the peri-pyloric and proximal part of the duodenum. The lesions in both organs were often multiple. The gastric lesions were composed of erosion and hyperplasia and those in the duodenum were exclusively hyperplasia. In mice given 0.4% and 0.1% HP for 420 to 740 days, 5 and 1% of them, respectively, had duodenal cancer by histological criteria though they did not show any distant metastasis. In the control group, no cancer was noted in the same observation period. The incidence and av numbers of lesions in both the stomach and duodenum after 150 to 210 days of HP intake decreased or fell to zero if HP administration was interrupted for 10 to 30 days. In DBA and BALB mice given 0.4% HP for 90 to 210 days, the incidences of gastric lesions reached 30 and 10% at max, respectively, and the incidences of duodenal lesions were 60 to 100% and 40 to 69%, respectively. (Author abstract) (17 Refs)

MECHANISMS AND MODIFICATIONS OF GI CARCINOGENESIS

23. INHIBITION OF THE HEPATOCARCINOGENIC ACTIVITY OF DIETHYLNITROSAMINE (DENA) BY ETHANOL IN RATS.

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Hepatogastroenterology; 28(5):242-244 1981

Male Sprague-Dawley rats received 0.1 mg/kg of diethylnitrosamine orally 5 times a wk for life with or without additional subsequent administration of 5 ml/rat/day of a 25% aqueous solution of ethanol. The additional treatment with ethanol significantly reduced the induction of liver cancer, but not of esophageal tumors. These findings do not support speculations based on epidemiologic studies as to a cancer-causing effect of alcohol. (Author abstract) (11 Refs)

24. OPERATION-SEQUEL CARCINOMA - AN EXPERIMENTAL STUDY.

Langhans P, Heger RA, Hohenstein J, Bunte H
Chirurgische Klinik der Universitat, Jungeblodtplatz 1, D-4400 Munster, W. Germany
Hepatogastroenterology; 28(1):34-37 1981

Gastric-stump carcinoma, a special form of gastric carcinoma, is seen as a late complication of gastric surgery performed on the carcinoma-free stomach. In the present experimental series a considerable number of carcinomas were observed, for the first time, in rats after gastric surgery without additional application of a carcinogen. The rate of malignancies arising in the gastric stump correlates closely with the intensity of the duodenogastric reflux provoked by different surgical procedures. The important role of duodenogastric reflux for the development and growth of gastric stump carcinoma is thus established beyond doubt. While bearing in mind the need for caution in translating experimental results to man, this study does suggest the value of reflux-preventing techniques in the surgical management of gastric diseases. Patients who have undergone an operation are at increased risk of developing carcinoma, and therefore require consequent and regular follow-up examination. The introduction of surgical prophylaxis and careful postoperative surveillance are the only effective methods for the prevention of gastric stump carcinoma. (Author abstract) (5 Refs)

25. CARCINOGENESIS AFTER EXPERIMENTAL VAGOTOMY: A LONG-TERM STUDY IN ANIMALS.

Stegemann B
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Fortschr Med; 100(13):596-591 1982

Possible carcinogenesis after nonresective gastric surgery was studied. Long-term observations were made of 560 female Wistar rats following surgery. Surgical procedures included truncal vagotomy (TV) with or without pyloroplasty (PP), selective proximal vagotomy (SPV) with or without PP, PP alone, severance of the left gastric artery, TV + PP with duodenogastrostomy in the papillary region (DGP), DGP without TV + PP, TV with resection of the antrum, and control sham operations. Half of all animals received the carcinogen N-methyl-N'-nitro-N-nitrosoguanidine (MNNG: 1.48 g/animal) in drinking water for 7 mo beginning 7 wk after surgery; MNNG provided for a comparison of animals with or without exposure to a carcinogenic compound. Overall survival rate was 65.5%; after 390 +-7 days 367 rats were evaluated. Carcinomas were found in 6% of rats that underwent TV + PP wihout MNNG and 8% of rats that underwent SPV + PP without MNNG. Carcinomas were also found in rats that underwent TV + PP with DGP or DGP alone. Cancers developed only at a pH greater than 4 (normal pH was 2-3). Morphological changes noted in test animals included atrophy of the gastric mucosa, achlorhydria, ulceration, and, after drainage surgery, duodenogastric reflux. Results suggest that vagotomy in humans, particularly with drainage procedures, carries a risk of carcinogenesis Careful postoperative surveillance is therefore required for patients undergoing nonresective gastric surgery. (28 Refs) (In GER)

26. DIMETHYLHYDRAZINE-INDUCED COLONIC NEOPLASIA: DISSOCIATION FROM ENDOGENOUS GASTRIN LEVELS.

Oscarson JE, Veen HF, Ross JS, Malt RA
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Surgery; 91(5):525-530 1982

The potential tropic effect of gastrin in promoting colonic carcinogenesis was tested in rats (n = 133) with 6-to 16-fold variations in endogenous gastrin resulting from antrectomy or fundectomy, followed by 12 injections of 1,2-dimethylhydrazine (10 mg/kg). The incidence and grade of differentiation of resulting tumors, as well as the thickness, content of nucleic acids, and specific activity of DNA in colonic mucosa, were similar in both high-gastrin and low-gastrin animals and were unchanged from data in unoperated control animals receiving only the carcinogen. Long-term changes in endogenous gastrin concentration are not followed by colonic mucosal tropic effects, and gastrin does not act as a cofactor in dimethylhydrazine-induced carcinogenesis at this dosage. (Author abstract) (25 Refs)

27. TUMOR DEVELOPMENT IN THE HUMAN COLON IS ENHANCED BY EPIDERMAL GROWTH FACTOR (UROGASTRONE), DEOXYCHOLIC ACID, AND AN ENDOGENOUS ANALOG TO TPA (MEETING ABSTRACT)

Friedman EA
Memorial Sloan-Kettering Cancer Center, New York, NY
Conference on Cell Proliferation, Cancer and Cancer Therapy, February 17-19, 1982, New York, New York New York Academy of Sciences; :AP-5 1982

Many human neoplasms arise through a series of progressive cellular changes. Premalignant cells in the colon form a benign tumor or adenoma, from which a carcinoma develops. Benign tumors fall into three classes based on their pathology and clinical prognosis. Premalignant epithelial cells cultured from each class reflect the tumor's position in the progression to carcinoma. Cells from early-stage (tubular) adenomas are stimulated to divide by EGF(epidermal growth factor) (structurally similar to urogastrone, a tropic hormone in the intestine), by TPA (12-O-tetradecanoylphorbol-13-acetate), and by deoxycholic acid, a secondary bile acid found in the colon. Cells from either intermediate-stage (villotubular) or late-stage (villous) adenomas are not stimulated to divide by EGF or by deoxycholic acid. TPA-treated intermediate and late-stage premalignant cells from rills and clusters several cells in thickness and secrete a plasminogen activator. This multilayering is reminiscent of areas of carcinoma found within adenomas. Furthermore, it suggests that a endogenous compound which binds to TPA receptors on late-stage premalignant cells, and so mimics TPA activity, is important in the transition to malignancy. (no Refs)

28. MECHANISM OF ORGAN-SPECIFIC TUMOR INDUCTION IN THE GASTRO-INTESTINAL TRACT (MEETING ABSTRACT)

Kleihues P
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J Cancer Res Clin Oncol; 103(Suppl):A11 1982

The metabolism and reaction with DNA of three carcinogens was investigated after systemic administration selectively induced tumors in different segments of the gastro-intestinal tract. These agents share a common ultimate carcinogen, methyl diazonium ion, and produce an identical pattern of methylated DNA bases. Following oral or systemic administration in rats, N-nitrosomethylbenzylamine (MBN) induced a high incidence of esophageal carcinomas. Methylation of DNA purines by a single iv dose of (methyl-14C) MBN is most extensive in the esophagus, followed by liver, lung and forestromach. In mice, systemic application of MBN resulted in the development of forestomach carcinomas as in this species, DNA methylation by MBN is higher in forestomach than in esophageal DNA. The alternative possibility of enzymic hydroxylation of the methyl group of MBN cannot be ruled out but after administration of (methylene-14C) MBN no benzylated DNA bases were detected in rat tissues. Methyl(acetoxymethyl)nitrosamine (DMN-OAc) is a stable derivative of the alpha-hydroxy intermediate of dimethylnitrosamine. Heterolytic decomposition of DMN-OAc occurs through esterase mediated cleavage of the acetoxy moiety. Following iv injection of (14C)DMN-OAc by far the highest levels of DNA alkylation were found in the lung, the principal target organ for this route of application. In contrast, ip injection of (14C) CMN-OAc resulted with a preferential alkylation of organs bordering the abdominal cavity with highest values in ileum and colon, the target organs for this route of application. Weekly sc injection of 1,2-dimethylhydrazine (DMH) in rats and mice cause a selective induction of colon carcinomas. Alkylation of DNA purines by DMH was highest in liver, followed by colon, kidney and ileum. (no Refs)

29. THE ACUTE EFFECT OF BETA-SITOSTEROL ON COLONIC EPITHELIAL CELL PROLIFERATION: IMPLICATIONS FOR MNU-INDUCED NEOPLASIA (MEETING ABSTRACT)

Deschner EE, Cohen BI, Raicht RF
Memorial Sloan-Kettering Cancer Center, New York, NY
Cell Tissue Kinet; 15(1):102 1982

The effect of dietary supplementation with beta-sitosterol (0.2% of diet) was followed in Fisher rats after a period of 3 and 7 days feeding. Compared with controls, the number of epithelial cells per crypt column in both plant sterol fed groups was shifted to lower values; moreover, fewer epithelial cells above cell position 12 were engaged in DNA synthesis. Rats treated with MNU (methylnitrosourea) intrarectally (2 mg) while consuming beta-sitosterol demonstrated a reduction in the number of [3H]TdR (thymidine) labelled cells per crypt column from that seen in rodents receiving just the carcinogen. Twenty-six weeks later, MNU-treated rats fed beta-sitosterol showed a significantly decreased colonic tumor incidence (1.3 tumor per tumor-bearing animal vs 2.1 tumor per tumor-bearing animal). This plant sterol which passes through the digestive tract relatively unabsorbed appears to slow colonic epithelial cell proliferation resulting in a reduced expression of neoplastic transformation. (1 Ref)

30. THE INTESTINAL ENZYMATIC BIOTRANSFORMATION SYSTEM: POTENTIAL ROLE IN PROTECTION FROM COLON CANCER.

Hoensch HP, Hartmann F
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Hepatogastroenterology; 28(4):221-228 1981

Neutralization of lipophilic dietary toxins through biotransformation is reviewed in relation to protection from colon cancer. While the liver is important for biotransformation of certain drugs, the low-capacity biotransformation xenosystem of the gut may have a high affinity for dietary lipophilic chemicals which are present in low concentrations in the gut lumen. Topics discussed include the localization of the intestinal xenosystem, regulation of enzyme activity, relationship to carcinogenesis, the human intestinal xenoenzyme system, and a model for cancer protection. (76 Refs)

31. INTERFERENCE WITH DIMETHYLHYDRAZINE INDUCTION OF COLON TUMORS IN MICE BY EPSILON-AMINOCAPROIC ACID.

Corasanti JG, Hobika GH, Markus G
Dept. Experimental Biology, Roswell Park Memorial Inst., New York State Dept. Health, Buffalo, NY, 14263
Science; 216(4549):1020-1021 1982

The antifibrinolytic agent epsilon-aminocaproic acid given in the drinking water to Swiss ICR/Ha mice significantly counteracted the appearance of colorectal tumors induced by 21 weekly injections of 1,2-dimethylhydrazine. The drug affected both the number and the location of the tumors and, in some animals, altogether prevented their appearance. The low concentrations of epsilon-aminocaproic acid in the plasma of four control mice given the agent labeled with carbon-14 for 3 days suggest that the effect may depend not on inhibition of plasminogen activator activity, but on interference with the binding of some substance to the strong lysine binding site of plasminogen. (Author abstract) (29 Refs)

32. THE BIOLOGICAL EFFECTS OF CARRAGEENAN AND OTHER SULFATED POLYSACCHARIDES WITH PARTICULAR ATTENTION TO IMMUNOLOGICAL AND CARCINOGENIC PROPERTIES.

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Ugeskr Laeger; 144(12):860-863 1982

A review of studies on the biological effects of carrageenan shows that induction of colorectal cancer was observed in rats following long-term oral administration of degraded carrageenan. Native (high-molecular-weight) is not known to possess carcinogenic properties. Carrageenan stimulates tumor growth secondarily. The cocarcinogenic effect of carrageenan may be due to its immunosuppressive properties (toxic effect on macrophages and activation of macrophage suppressor cells). (29 Refs) (In DAN)

33. PROTECTIVE EFFECT OF NICOTINAMIDE ON BRACKEN FERN INDUCED CARCINOGENICITY IN RATS.

Pamukcu AM, Milli U, Bryan GT
Div. Clinical Oncology, Dept. Human Oncology, Wisconsin Clinical Cancer Center, K4/554, CSC, 600 Highland Ave., Madison, WI, 53792
Nutr Cancer; 3(2):86-93 1981

Albino noninbred weanling male and female rats were fed a basic grain diet (Group 1), a basic diet supplemented with 0.5% nicotinamide (Group 2), a basic diet containing 33% bracken fern (BF) (Group 3), or a basic diet supplemented with 33% BF and 0.5% nicotinamide (Group 4) for 58 wk. Dietary nicotinamide decreased the BF-induced incidence of both intestinal and bladder tumorigenesis by about 40%. The inhibitory effect of nicotinamide on the BF-induced intestinal and bladder tumors was significant at p less than 0.05 and p less than 0.01, respectively. (Author abstract) (39 Refs)

34. EFFECT OF ESTRADIOL PROPIONATE AND PREGNANCY ON CARCINOGENESIS INDUCED BY 1,2-DIMETHYLHYDRAZINE IN C3HA MICE.

Turusov VS, Murovannyi AN, Morozova OV
All-Union Cancer Res. Center, Moscow, USSR
Eksp Onkol; 4(2):20-23 1982

The effects of pregnancy and estradiol propionate (EP) administration on 1,2-dimethyl hydrazine (DMH)-induced carcinogenesis were studied in female C3HA mice. Virgin or pregnant females were subjected to sc administrations of DMH (8 mg/kg/wk) alone or in combination with EP (10 ug/kg/wk). DMH and EP were given for 30 wk. Animals were followed up for 50 wk after the initiation of the experiment. DMH alone induced tumors in 75% of virgin mice and in 56.2% of pregnant mice. EP administration resulted in a marked increase of the incidence of colonic tumors (31.6%, compared with 8.3% after administration of DMH alone to virgin mice and 18.7% after administration of DMH alone to pregnant mice). Uterine sarcomas were observed in 28.9% of mice treated with DMH + EP, while all mice treated with DMH alone were free of uterine sarcomas. Hepatocellular tumors were observed only in mice treated with DMH + EP (23.7%). These findings indicate that EP can modify the DMH-induced carcinogenesis not only in the hormone dependent organs but also in the liver and in the colon. (14 Refs) (In RUS)

35. NICOTINE INFLUENCE UPON THE DEVELOPMENT OF EXPERIMENTAL STOMACH TUMORS.

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Lab. Carcinogenic Agents, Petrov Res. Inst. Oncology, 68 Leningradskaya St., Pesochny-2, Leningrad 188646, USSR

Arch Geschwulstforsch; 52(4):259-265 1982

The ability of nicotine (NC) to modify the carcinogenic effect of N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) was studied in rats. Eighty-five male random bred white rats were divided into two series. The total MNNG dose was av 162.7 mg/animal in the Group 1 of the first series and 166.2 mg/animal in Group 2 of the first series. Group 2 animals also received 0.5 mg/kg NC sc 3x/wk. Group 3 animals (genetic controls) received neither MNNG nor NC. The 25 rats in the second series were studied for acetylcholinesterase activity in cerebrum, hypothalamus, and medulla. Rat stomach wall slices were studied microscopically. After several wk, the specific sequential structural modifications of glands developed, accompanied by persistent non-specific changes, in MNNG-exposed rats. Different signs of non-specific changes were observed in stomachs of all Group 1 and Group 2 rats. The simplification of glandular structure was marked. A number of rats in Groups 1 and 2 showed signs of buds and shoots developing in the middle and basal parts of the wall glands. These changes were accompanied by the formation of short branching and cystically epithelial complexes with signs of atypia. Fifty percent of Group 1 and 67% of Group 2 rats showed more advanced changes of epithelial complexes sprouting into the stomach wall. Malignization and formation of adenocarcinomas were observed in all such cases. The multicentric character of the induced specific pathological changes was especially well expressed in Group 2 animals. No spontaneous precancerous changes or cancer of the stomach were found in Group 3 rats. Results showed that animals subjected to the combined MNNG and NC treatment developed stomach cancers earlier and at double the frequency of control animals. NC enhanced the carcinogenic effect of MNNG. (30 Refs)

BIOCHEMICAL, MORPHOLOGICAL AND IMMUNOLOGICAL ASPECTS OF GI CARCINOGENESIS

36. PATHOGENESIS OF 1,2-DIMETHYLHYDRAZINE-INDUCED CARCINOMAS IN RAT INTESTINE. II. HISTOCHEMICAL AND ULTRASTRUCTURAL CHARACTERISTICS OF GLYCOPROTEINS OF 1,2-DIMETHYLHYDRAZINE-INDUCED CARCINOMA CELLS.

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Acta Pathol Jpn; 32(2):265-279 1982

Two hundred twenty seven lesions of DMH-induced intestinal carcinomas of 68 male Wistar rats were investigated by means of histochemical and electron microscopic properties to study their histogenesis and mucinogenesis. Among the epithelial glycoproteins, surface glycoprotein on the microvilli with glycocalyces was distinguishable from mucin in the cytoplasm based on histochemical staining and ultrastructural findings. From the phenotypic characteristics of glycoproteins, it was suggested that DMH-induced carcinomas could be classified into mucin producing carcinomas composed mainly of cells containing intracellular mucins and non-mucin producing ones. The mucin producing carcinomas consisted of poorly differentiated adenocarcinoma, signet ring cell carcinoma, and mucinous carcinoma presumably resulting from various degrees of differentiation into goblet cells. Their staining attitude varied and cells with neutral mucin, sialomucin and sulfated mucin were observed in the signet ring cell carcinoma. In addition, abnormal synthesis of glycoproteins was observed with ConA-paradox staining and PATS/PB/KOH/PAS. These histochemical properties suggested irregular synthesis of glycoproteins in carcinomas. In non-mucin producing carcinomas, glycoproteins were found mainly on the apical surface and contained sialomucin. A deviated differentiation into an absorptive cell could form an intracytoplasmic cyst filled with an aggregation of glycocalyces, so becoming another type of signet ring cell. (Author abstract) (28 Refs)

37. BIOCHEMICAL AND HISTOPATHOLOGICAL RESPONSE TO CHRYSOTILE INGESTION IN GUINEA PIGS.

Saxena KC, Srivastava L, Dogra RK
Industrial Toxicology Res. Centre, Mahatma Gandhi Marg, Post Office Box 80, Lucknow 226001, India
Ind Health; 20(1):19-25 1982

The biochemical and histopathological changes induced by ingested asbestos (chrysotile dust, 500 mg) were studied in guinea pigs over a period of 24 hr. A significant increase in the volume of gastric juice, free and total acidity, and peptic activity associated with a decrease in the mucin content of gastric juice, after chrysotile ingestion, indicates that these changes may be related to the dissolution and/or disposal of chrysotile dust in the stomach. Most changes occurred at 12 hr, the period of maximal dissolution of chrysotile dust as evidenced by the leaching of nickel. A rise in ATPase activity of the gastric mucosa also occurred at 12 and 24 hr. Damage to the mucosal cells was evident histopathologically 12 hr after chrysolite ingestion, and was probably due to the injury (erosion or penetration) caused by the asbestos fiber in the gastric mucosa. Restoration and reversal of changes in volume, free acidity, gastric juice mucin content, and gastric mucosal injury occurred at 24 hr. Apparently this occurred because most of the chrysotile had been expelled from the stomach. The role of gastric juice acidity and nickel dissolution in the production of gastric ulceration and carcinoma from ingested chrysotile were discussed. (22 Refs)

38. COMPARATIVE HISTOCHEMICAL OBSERVATIONS ON THE CHANGES OF MUCOSUBSTANCES IN FETAL GASTRIC MUCOSA AND GASTRIC ADENOCARCINOMA.

Hou J
Dept. Histology and Embryology, Lanzhou Medical Coll., Lanzhou, People's Republic of China
Acta Anat Sin; 12(3):304-309 1981

Changes of mucosubstances (mucopolysaccharide, neutral mucin) are described for the gastric mucosa of 16 fetuses (11 males, 5 females; 11 wk to full term), 5 cases of gastric adenocarcinoma, 1 case of gastritis and 1 normal adult. The mucosubstances of the fetal gastric mucosa were found to change from acidic to neutral during the course of fetal development. However, some acidic mucosubstances were also found in adults as well as in gastric adenocarcinoma. (17 Refs) (In CHI)

39. PATHOGENESIS OF 1,2-DIMETHYLHYDRAZINE-INDUCED CARCINOMAS IN RAT INTESTINE. 1. THE INDUCTION OF MUCIN PRODUCING CARCINOMAS IN RAT INTESTINE.

Takiemiya M, Miyayama H, Takeuchi T
Dept. Pathology, Kumamoto Univ. Sch. Medicine, 2-2-1 Honjo, Kumamoto 860, Japan
Acta Pathol Jpn; 32(2):257-264 1982

Seventy four white male Wistar rats were divided into two groups and given weekly subcutaneous injections of 30 mg 1,2-dimethylhydrazine (DMH) 2HCl/kg body weight for 10 or 15 weeks, respectively, and the histological properties and distribution of DMH-induced rat carcinomas were investigated. The carcinomas induced by DMH were classified mainly into mucin producing carcinomas and non-mucin producing ones. In the large intestine, the group treated for 15 weeks induced significant incidences of mucin producing carcinomas composed mainly of cells containing intracellular mucin. Mucin producing carcinomas consisted of poorly differentiated adenocarcinoma, signet ring cell carcinoma and mucinous carcinoma, and these often coexisted within the same tumor mass. Mucin producing carcinomas tended to develop in the proximal colon and cecum, while non-mucin producing carcinomas were frequent in the distal colon. This method was thought to be a useful model to study glycoproteins of cancer cells. (Author abstract) (17 Refs)

40. HISTOPATHOLOGY OF EARLY STAGES IN EXPERIMENTAL GASTRIC CARCINOMA (MEETING ABSTRACT)

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J Cancer Res Clin Oncol; 103(Suppl):A12 1982

Since the reports of Sugimura et al (1967) on the carcinogenicity of N-methyl-N-'-nitro-N-nitrosoguanidine (MNNG), numerous authors have published a wealth of histopathologic data on chemically induced gastric carcinoma. However, interpretation and classification of histologic findings in pre-cancerous and pre-invasive stages of experimental gastric cancer are still far from coherent. Combined with a review of findings documented in the literature, the analysis of our own extensive studies resulted in a concept of three possible modes of carcinoma development: 1) lumen-oriented hyperplasia (exophytic adenomatous growth) leading to polypous adenocarcinoma; 2) serosa-oriented adenomatous proliferation (hyperplasia) with increasing cellular atypia leading to infiltration and transformation into carcinoma; 3) direct invasion of atypical 'tumor cells' into the mucosal stroma unpreceded by mucosal hyperplasia. The specific features of carcinogenesis in the operated stomach reflect the change in anatomical conditions provoked by the surgical traumatization of the mucosa, and the resulting change of proliferation kinetics. Experimental data on the stages of carcinogenesis may be compared with analogous findings in the human stomach after gastric surgery. (no Refs)

41. IN VITRO CHARACTERIZATION OF GARDNER SYNDROME, FAMILIAL POLYPOSIS COLI, HEREDITARY DISCRETE COLORECTAL ADENOMAS, AND COLORECTAL CARCINOMA (MEETING ABSTRACT)

Gardner E, Burt R, Edward S, Neff L
Utah State University, Salt Lake City, UT
Am J Hum Gen; 33(6):63A 1982

Samples from large kindreds with Gardner syndrome (K 109), familial polyposis coli (K 267, K 268, and K 269), hereditary discrete colorectal adenomas (K 133), and individuals with invasive or recurrent colorectal carcinoma have been obtained. The samples include skin biopsies from the upper arm for fibroblast culture, adenoma biopsies from upper and lower Gastrointestinal tract with flexible endoscopes for fibroblast culture, and peripheral blood for mutagen challenge and sister chromatid exchange. Fibroblast cultures have been characterized for saturation density and growth on different levels of fetal calf serum. Fibroblast chromosomes have been G-banded, karyotyped, and characterized for structural and numerical instability, polymorphism in chromosome number 2, mutagen challenge, and sister chromatid exchange. More than 100 fibroblast lines have been frozen for future use and futher comparsions. Lymphocyte chromosomes have been G-banded, mutagen challenged, and scored for sister chromatid exchange. With these tests, different polypoid and cancerous conditions are distinguished in vitro on the basis of cell culture and chromosome criteria. Random chromosome instability and chromosome number 2 heteromorphism data will distinguish Gardner syndrome and familial-polyposis coli patients from those with hereditary discrete polyps and normal controls. Response of sister chromatid exchange with mitomycin-C mutagen challenge will distinguish Gardner syndrome, invasive colon cancer, recurrent colon cancer, hereditary discrete polyp patients, and controls for each other. (no Refs)

42. MORPHOLOGIC ANALOGY OF INTESTINAL TRACT CARCINOGENESIS IN ADENOMATOUS POLYPOSIS AND THE AZOXYMETHANE-TREATED RAT MODEL (MEETING ABSTRACT)

Hamilton SR, Stephens RB, Natuzzi E, Boitnott JK, Yardley JH
Departments of Pathology and Surgery, The Johns Hopkins University School of Medicine and Hospital, Baltimore, MD
Lab Invest; 46(1):33A 1982

Parenteral administration to rodents of azoxymethane (AOM), a metabolite of dimethylhydrazine, provides a widely used model of colonic carcinogenesis. Unlike usual large bowel carcinoma in human beings (ULBC) but analogous to adenomatous polyposis (AP), the AOM model has a high incidence of multiple colonic carcinomas and proximal small bowel carcinomas, particularly with higher dosage of carcinogen. In this study, grossly normal colonic mucosa from 10 resectons for

ULBC, six prophylactic colectomies for AP, four AOM-treated, and four control rats was examined for dysplastic crypts in en face histologic sections oriented in the plane of the luminal surface. AOM-treated rats were male Fischer 344 rats given 10 weekly subcutaneous injections of 7 mg of AOM per kg, starting at 11 weeks of age and killed 24 weeks after the first dose. Grossly normal colonic mucosa showed 0.03 foci of dysplastic crypts per sq cm examined in ULBC, 3.0 in AP, 2.9 in AOM rats, and 0.05 in control rats. Dysplastic crypts composed 0.005 per 1000 crypts examined from right colon in ULBC, 39 in AP, and 0.3 in AOM rats, intermediated to AP and ULBC rats. The presence of multifocal dysplastic crypts in grossly normal colonic and small bowel mucosa of the AOM model provides additional evidence of a generalized intestinal tract carcinoma diathesis which is more analogous to adenomatous polyposis than usual large bowel cancer. (no Refs)

43. METABOLISM OF N'-NITROSONORNICOTINE BY CULTURED RAT ESOPHAGUS.

Hecht SS, Reiss B, Lin D, Williams GM
Naylor Dana Inst. Disease Prevention, American Health Foundation, Valhalla, NY, 10595
Carcinogenesis; 3(4):453-456 1982

The metabolism of N'-nitrosonornicotine (NNN), an esophageal carcinogen, by organ cultured F-344 rat esophagus was investigated. The major metabolites were separated by hplc and were identified by comparison to standards as 4-hydroxy-1-(3-pyridyl)-1-butanone, 4-hydroxy-4-(3-pyridyl)-1-butanol and 4-oxo-4-(3-pyridyl)butyric acid from 2'-hydroxylation of NNN and 4-hydroxy-4-(3-pyridyl)butyric acid from 5'-hydroxylation of NNN. These results demonstrate that alpha-hydroxylation, which leads to electrophilic diazohydroxides, is the major pathway of metabolism of NNN in cultured F-344 rat esophagus. The extents of formation of the metabolites increased with time and the ratio of products resulting from 2'-hydroxylation to those resulting from 5'-hydroxylation was 4.3 after 1 hr, 3.9 after 6 hr, 3.4 after 24 hr and 3.1 after 48 hr. F-344 rat liver slices from the same animals produced metabolites of NNN with a 2'/5'-hydroxylation ratio of 1.4. The 2'/5'-hydroxylation ratio in cultured Syrian golden hamster esophagus was 0.3. These results, together with those of parallel studies of NNN metabolism in A/J mouse lung and Syrian golden hamster trachea indicate that among these tissues, F-344 rat esophagus has a unique ability to preferentially hydroxylate the 2'-position of NNN. The results suggest that 2'-hydroxylation is the key step in the metabolic activation of NNN in rat esophagus. (Author abstract) (18 Refs)

44. ENZYMATIC CHARACTERISTICS OF TUBULAR ADENOMAS AND CARCINOMAS OF THE LARGE INTESTINE.

Vatn MH, Tjora S, Arva PH, Serck-Hanssen A, Stromme JH
Med A, Rikshospitalet, Oslo 1, Norway
Gut; 23(3):194-197 1982

Enzyme activities in homogenates of the large intestine were measured in biopsies from 11 tubular adenomas and 6 carcinomas and from the corresponding normal mucosa of each individual. A similar and significant increase was found in the total activities of glucose-6-phosphate dehydrogenase (G 6 PD), pyruvate kinase, and lactate dehydrogenase in adenomas and carcinomas as compared with levels of normal mucosa. The lactate dehydrogenase isoenzyme patterns showed also a marked and similar change in the adenomas and carcinomas with a significant increase of lactate dehydrogenase M-monomers. Most of the adenomas showed slight to moderate dysplasia. The results indicate that the measurement of total G 6 PD, pyruvate kinase and lactate dehydrogenase activities for screening purposes has no predictive value in separating nonpremalignant from premalignant adenomas. Moreover, it seems that the enzymatic characteristics of malignancy are present even in tubular adenomas. This is in agreement with the theory of a polyp-cancer sequence. (Author abstract) (25 Refs)

45. MONOCLONAL ANTIBODY DEFINED ANTIGENS OF GASTRO-INTESTINAL TUMORS (MEETING ABSTRACT)

Steplewski Z, Koprowski H
The Wistar Institute, Philadelphia, PA, 19104
Fed Proc; 41(3):726 1982

Several of hybridoma-secreted anti-gastro-intestinal (GI) cancer monoclonal antibodies bind specifically to cultured in vitro cells of colorectal, gastric and pancreatic carcinomas. Other tumors and normal fibroblasts maintained in tissue culture do not react with these antibodies. Peripheral blood lymphocytes or EBV-transformed lymphocytes were also unable to bind these antibodies. Monoclonal antibodies 19-9, 52a, and C4 14 detect antigens released by tumor cells cultured in vitro. Antigen detected by antibodies 19-9 and 52a was detected in the serum of patients with GI cancer: 163 of 255 patients with colorectal carcinoma, 45 of 49 patients with pancreatic carcinoma, and 8 of 11 patients with gastric carcinoma. In immunoperoxidase assay the antigen was found in 51% of colonic adenocarcinomas, 82% of pancreatic adenocarcinomas and 100% of gastric carcinomas. Hybridomas established after immunization with freshly isolated tumor cells, secreted monoclonal antibodies directed against a variety of other glycolipid antigens, including blood group antigens. They include Leb antigen, and two types of precursor substances common to the ABH and Lewis system: type 1 with beta1.3 linkage and type 2 with beta1.4 linkage of terminal galactose to N-acetylglucosamine. Another four antibodies react with blood group B substances. Four antibodies are directed against a fucosyl-paragloboside. (no Refs)

46. IMMUNOLOGICAL PROPERTIES OF IN VITRO PASSAGED CARCINOMAS AND PROPAGATED CLONES FROM DIFFERENT CELL LINES (MEETING ABSTRACT)

Jamasbi RJ, Perkins EH
Antaeus Research Institute, Fayetteville, AR, 72701
Proc Am Assoc Cancer Res; 23:1064 1982

DEN (Diethylnitrosamine)-induced forestomach carcinomas of BALB/c mice are non- or very weakly immunogenic. However, cultured cell lines established from these tumors showed increased immunogenicity, ie, some DEN-induced cell lines lose their tumorigenicity at early passages; others did not lose it up to the 30-50th passages (the highest passages tested). We also observed significant cellular heterogenicity among tumors of the same origin and within the same primary tumor cell line. To determine the degree of cellular heterogeneity among cell lines and if sub-populations of lower tumorigenic cells show selective growth over more tumorigenic cells, we isolated 20 clones from each cell line using early in vitro passages (2-5). Some of the isolated clones failed and some appeared microscopically identical. Generally 3-8 clones from each line grew and demonstrated that different clones show different degrees of tumorigenicity, immunogenicity and invasiveness. The in vitro growth properties of clones isolated from the same primary tumor were also quite different. The more tumorigenic, less immunogenic, metastasizing clones showed significantly lower seeding efficiency, whereas their growth rate and doubling time when they finally attached to the surface of culture dishes were significantly higher than their less tumorigenic, more immunogenic, non-metastasizing counterparts. (no Refs)

47. NMR RELAXATION TIMES OF WATER PROTONS IN HUMAN COLON CANCER CELL LINES AND CLONES.

Beall PT, Hazlewood CF, Rutzky LD
(c/o Rutzky) Dept. Surgery, Biochemistry and Molecular Biology, Univ. Texas Medical Sch., Houston, TX, 77030
Cancer Biochem Biophys; 6(1):7-12 1982

Established lines of human colon cancer cells from several sources (LS180, LS174T, HT29, SW480, SW1345) had water proton nuclear magnetic resonance (NMR) spin-lattice relaxation times (T1) of 460 +-45 msec to 982 +-9 msec and spin-spin relaxation times (T2) of 83 +-6 msec to 176 +-6 msec. Two clones derived from single cells of line LS174T were similar in T1 and T2 to the parent line. Differences among the cell lines were not totally a function of cellular hydration. Normal adult and fetal human primary colon cells were wetter and had higher T1 and T2 values than established cell lines. Relaxation times in this study substantiate variations seen for human colon tumors in earlier studies. Established cell lines maintained water relaxation times similar to tumor tissue values. Along with other morphological and biochemical criteria, the relaxation times suggest that these established human colon cancer cell lines may serve as a good experimental model for the study of human colon cancer. (Author abstract) (44 Refs)

48. BLOOD GROUP ANTIGENS AND GASTRIC CANCER.

Feizi T
Div. Communicable Diseases, Watford Road, Clinical Res. Centre, Harrow, Middlesex HA1 3UJ, England
Med Biol; 60(1):7-11 1982

Expression of the major blood group antigens in the superficial mucosa and the mucosal glycoproteins of the human stomach in health and in benign and malignant diseases of the stomach is reviewed. Disease associated changes occur and can be readily detected. The reason for changes in carbohydrate structures are not yet known, they may be due to deletions of the glycosyl transferases or a failure of their coordinated action. In wound healing a loss of blood group antigen A has been observed and in hematological disorders increased numbers of erythrocytes expressing i antigen are released into the blood stream. (24 Refs)

49. INVESTIGATION OF EARLY STAGE OF INTESTINAL METAPLASIA.

Tada M, Iida Y, Odawara M, Takeuchi K, Harada H, Saito M, Sataka M, Sakaki N, Goto K, Aonuma K, Okazaki Y, Kawamura S, Takemoto T, Ogino T, Sasaki K, Takahashi M
First Dept. Internal Medicine, Yamaguchi Univ. Sch. Medicine, Yamaguchi, Japan
Gastroenterol Endosc; 23(3):426-434 1981

Early stages of C-1 type gastric mucosa (Kimura-Takemoto classification) in 15 patients (8 males, 7 females, 15-64 yr old) were studied with respect to distribution of metaplasia, histological findings from biopsied specimens, enzyme activities, and cell kinetics using 3H-thymidine autoradiography. The occurrence of metaplasia was limited mostly to the prepyloric region (88%); the rest were in the antrum. Histologically, all were goblet cell metaplasia lacking paneth cells. Enzymatically, 4/15 cases were alkaline phosphatase positive and leucine aminopeptidase negative incomplete metaplasia. Autoradiographic findings showed an enlargement of the generative cell zone. Little difference in labeling index (LI) was observed between gastritis and early stage intestinal metaplasia and between the LI of young patients and older patients. It appears that the metaplasia found in C-1 type mucosa may be a good model for studying the early stage of metaplasia. (31 Refs) (In JPN)

PANCREATIC CARCINOGENESIS

50. FAMILY HISTORY AND ENDOMETRIAL CANCER (MEETING ABSTRACT)

Philippe P
University of Montreal, Quebec, Canada
Am J Hum Gen; 33(6):141A 1981

Preliminary results of a study designed to compare family history-positive (FH+) cases (with cancer of any site in 1st degree relatives) of endometrial cancer with their FH- counterparts (sporadic), are presented for the first 27 patients. The diagnosis of adenocarcinoma of the endometrium was confirmed in 26 probands (with one exception where a leiomyosarcoma was present); histopathological records of cancer in most 1st and 2nd degree relatives of probands were also searched. When compared to sporadic cases, FH+ probands proved to be less heavy and taller (thus less obese), were more fertile, had menarche later and were less frequently hypertensive. The FH+ group consistently showed more homogeneity on above features (except for family size) as pointed out by a lower variance. No difference, however, reached statistical significance. Despite low statistical power, the internal consistency of the results suggests that the classical epidemiological features of endometrial cancer more often pertain to its sporadic occurrence, thus reflecting a different physiopathological process. The relative rate of cancer in 1st and 2nd degree relatives of familial cases showed an excess of breast (19%), liver (11%), brain (8%), bone (8%) and pancreatic (8%) cancers, and a deficiency of lung cancers (8%). It is likely that the high prevalence of liver cancer is inflated (none confirmed yet) because of its highly metastatic nature. (1 Ref)

51. INHIBITION OF PANCREATIC CARCINOGENESIS BY RETINOIDS IN AZASERINE TREATED RATS (MEETING ABSTRACT)

Longnecker DS, Kuhlmann ET, Curphey TJ
Department of Pathology, Dartmouth Medical School, Hanover, NH, 03755
Fed Proc; 41(3):683 1982

Chemoprevention by retinoids of the progression of azaserine-induced carcinomas and preneoplastic lesions in rats was evaluated. Lewis rats were given 5 weekly injections of 30 mg/kg of azaserine while fed a chow diet, and then were fed chow supplemented with retinoids at the level of 0.5-2.0 mmol/kg diet for 1 year. The incidence of neoplasms was determined by autopsy and histologic study. The incidence of localized pancreatic carcinomas among a male positive control group (azaserine-treated, but not retinoid-treated) was 24% and in female group was 17%. The incidence of pancreatic carcinomas among male and female groups treated with N-4-pivaloyloxyphenyl retinamide was 4% and 0%, respectively. These were significantly below the control group incidence. Animals fed N-2-hydroxypropyl retinamide, N-3-hydroxypropyl retinamide (3HPR) and N-2,3-dihydroxypropyl retinamide (2,3HPR) showed a similar trend in both sexes but significance was reached only in the female groups fed the 3 HPR and 2,3HPR. Since retinoids were fed after exposure to carcinogen, the effect was exerted during the postinitiation phase of carcinogenesis. The ratio of localized and early invasive carcinomas to earlier precursor lesions was clearly higher among non-retinoid treated rats than among those treated with retinoids. This is consistent with an inhibition of progression in the retinoid-treated groups. (no Refs)

52. A FAMILIAL AGGREGATION OF PANCREATIC CANCER: AN IN VITRO STUDY.

Danes BS, Lynch HT
Lab. Cell Biology (D-209), Dept. Medicine, Cornell Medical Coll., 1300 York Ave., New York, NY, 10021
JAMA; 247(20):2798-2802 1982

The incidence of pancreatic cancer has been increasing steadily in the United States and other industrialized nations. Its obscure etiology and difficult early diagnosis tend to hobble effective control programs. Innovative methods, such as biomarkers, might provide clues to its inevitable occurrence in high-risk individuals. We studied a family in which four individuals manifested pancreatic cancer verified through two generations. Cell cultures from split-thickness skin biopsy specimens were obtained from 24 members from three generations (17 bloodline relatives, 7 family members by marriage) as well as 10 nonfamily normal subjects, none with a family history of solid tumors. One of the constant features of human monolayer dermal cultures has been diploidy. Hyperdiploidy, other than tetraploidy, has been rarely observed in cultures from normal subjects without a family history of solid tumors. We observed increased in vitro hyperdiploidy in 8 of 17 family members studied. (Author abstract) (33 Refs)

53. CHOLECYSTOKININ INHIBITS NITROSAMINE-INDUCED CARCINOGENESIS (MEETING ABSTRACT)

Johnson FE, LaRegina MC, Martin SA, Bashiti HM
St. Louis University Medical Center, St. Louis, MO
Joint Meeting of the Society of Surgical Oncology and Society of Head and Neck Surgeons, April 18-23, 1982, Marco Island, Florida. The Society of Surgical Oncology and the Society of Head and Neck Surgeons 265 pp., 1982.

Acute administration of cholecystokinin (CCK) has well-known effects on gall bladder contractions and pancreatic-biliary secretion. Recent data indicates that chronic administration of CCK has trophic effects on abdominal viscera, particularly pancreas. In order to determine whether CCK enhances malignant growth as well as growth of normal organs, we administered CCK together with di-isopropanol nitrosamine (DIPN), a carcinogen known to induce pancreatic, hepatic (and other) carcinomas. Two hundred young male Syrian golden hamsters (approx 60 gm) were divided into four groups. Group A (80 animals received DIPN (250 mg/kg) plus CCK (20 U/kg) by weekly subcutaneous injections; Group B (80 animals), DIPN alone; Group C (20 animals), CCK alone; Group D (20 animals), saline. Injections were done for 40 weeks, with animal sacrifice and autopsy at 10, 14, 18, 27, and 40 weeks. Microscopic study of pancreas, liver, heart, lung, brain, spleen small intestine, large intestine, testis, kidney, and stomach was carried out in each animal. Animal weights and visceral weights showed no striking differences between groups. Microscopic examination of the pancreas showed: DIPN induced pancreatic and hepatic carcinomas; CCK administration appeared to prevent their development. The mechanism of this effect is unknown. These results have implications for human carcinogenesis, and some of the implications are testable by currently available methods. (no Refs)

54. HISTOPATHOLOGICAL STUDY OF EARLY LESIONS OF PANCREATODUODENAL CANCER.

Miwa A, Kitagawa M, Tsuji M

Dept. Pathology, Toyama Medical and Pharmaceutical Univ., 2630 Sugitani, Toyama 430-01, Japan

Acta Pathol Jpn; 32(2):293-305 1982

The early lesions of pancreatoduodenal cancer, which was defined as those in which the site of origin in confined in a single certain anatomical part and the mode of early extension can be pursued, were found in 28 of 52 surgical specimens examined; 12 in the pancreatic portion of the common bile duct (PCBD), 12 in the common channel, 1 each in the terminal portion of the common bile duct and the terminal portion of the pancreatic duct, and 2 in the peripapillary zone of the duodenum. There were roughly two types of tumor growth; one annular flat-raised, histologically scirrhous tubular adenocarcinoma, principally found in PCBD and the other polypoid, histologically papillary or papillotubular adenocarcinoma, found everywhere. The staining properties of mucin was of no value in differential diagnosis for the site of origin. One typical carcinoid was observed in PCBD. The surface spread of carcinoma beyond the originating part was seen in 10 cases (36%), lymphatic invasion in 23 cases (82%), node metastasis in 9 cases (32%), and venous invasion in 6 cases (21%). Only two cases were mucosal carcinomas. From these figures it can be concluded that the carcinoma of this region is of high grade malignancy. (Author abstract) (8 Refs)

55. MORPHOLOGIC ANALYSIS OF ATYPICAL ACINAR CELL LESIONS (AACL) INDUCED IN RAT PANCREAS BY 4-HYDROXYAMINOQUINOLINE-1-OXIDE (4-HAQO) (MEETING ABSTRACT)

Rao MS, Upton MP, Subbarao V, Scarpelli DG

Department of Pathology, Northwestern University Medical, Chicago, IL, 60611

Fed Proc; 41(3):1547 1982

A metabolite of 4-nitroquinoline-1-oxide (4-HAQO), is both toxic and carcinogenic for pancreas. A single IV injection in male Wistar rats at a dose of 6 mg/kg bwt induced AACL in 100% of the animals. AACL could be classified histologically as zymogen-poor and zymogen-rich foci, and zymogen-rich nodules (grossly visible). The zymogen-poor foci contained 20-300 cells and rarely more than 500 cells. Cells in such foci were large, contained a large irregular nucleus with a prominent nucleolus, and a markedly basophilic cytoplasm with a few zymogen granules. By TEM (transmission electron microscopy) these cells showed markedly irregular lateral plasma membrane, and a well developed RER (rough endoplasmic reticulum). Cells in zymogen-rich foci and nodules were arranged in acini which were larger than adjacent ones, contained an intensely eosinophilic granular cytoplasm, and a large oval basophilic nucleus with a prominent nucleolus. These cells had a zymogen-rich cytoplasm, well developed RER, and irregular lateral membranes. Mitotic and [3H]thymidine labeling indices of both cell variants of AACL were as follows: eosinophilic cells, 2.75 and 23.2, basophilic cells 0.125 and 1.2 as compared to 0 to 1 for normal acinar cells. These studies indicate that 4-HAQO induces at least 2 variants of AACL with different morphological features and growth capacity. (no Refs)

56. DNA ADDUCT FORMATION IN HUMAN AND RAT PANCREATIC EXPLANTS TREATED WITH N-METHYL-N-NITROSOUREA (MNU) (MEETING ABSTRACT)

Friedman S, Parsa I

State University of New York, Downstate Medical Center, Brooklyn, NY, 11203

Fed Proc; 41(3):1548 1982

To evaluate the carcinogenic process in an in vitro model of pancreatic carcinogenesis the early effects of carcinogens on pancreatic explants in organ culture were studied. We have reported that adult human pancreatic explants can be transformed in organ culture by treatment with MNU. Since adduct formation of carcinogens with DNA is believed to play a role in carcinogenesis and is a measure of the reactivity of carcinogens with cellular macromolecules we have examined the reaction products of this alkylating agent with DNA under conditions, in organ culture, which cause the transformation of human pancreatic explants. Explants were exposed to 14C-MNU for 2 hours in a chemically defined medium. Total DNA was extracted by a modification of the method of Marmur and the purines analyzed after hydrolysis of the DNA in 0.1 M HCl at 70 degrees for 30 min by chromatography on Sephadex G-10. The analysis of methylated purine bases formed in the DNA of human pancreas indicates the formation of 1-methyladenine (0.0045 bases/1000 parent base), 3-methyladenine (0.0210), 7-methyladenine (0.0093), 7-methylguanine (0.239) and 06-methylguanine (0.024). MNU is approximately 1/10 as active in alkylating DNA of rat pancreatic explants as it is in alkylating DNA of human pancreas. (no Refs)

57. COMPARISON OF THE EFFECTS OF METHYLNITROSOUREA (MNU) ON ORGAN-CULTURED HUMAN AND RAT PANCREAS (MEETING ABSTRACT)

Parsa I, Butt KM

State University of New York Downstate Medical Center, Brooklyn, NY, 11203

Fed Proc; 41(3):379 1982

Organ-cultured adult human pancreas explants prepared from 10 cadaveric donors and in vitro differentiated embryonic rat pancreas were exposed twice a week to 1ug/ml of MNU in a chemically defined medium and cultured for up to 12 weeks. Twice a week rat and human explants were examined by light and electron microscopy to evaluate proliferation, hyperplasia, and carcinoma in ductal epithelium and in cells within the acinar complex. Early non-specific changes, degeneration of organelles, were present in all cell types of both species. Acinar cell necrosis was more prevalent in rat (89%) than in human explants (42%) and peaked by the end of the first week. Ductal cell proliferation and hyperplasia dominated the explant morphology in rat but were also common in human explants. Carcinoma, often in multiple foci, appeared as early as 6 weeks in rat and within 10-12 weeks in human explants. By the end of 12 weeks of treatment human explants showed carcinoma arising in ductal epithelium (20%) and in cells within the acinar complex (40%). More than 50% of rat pancreas explants developed carcinoma. Malignant cells in rat explants appeared to arise from cells devoid of zymogen and to form papillations composed of cells with extensive interdigitation of plasma membranes and an abundance of tono-filaments and tono-fibers, consistent with ductal cell carcinoma. (no Refs)

58. PANCREATIC CARCINOMA INDUCED BY N-METHYL-N'-NITROSOUREA IN AGED MICE.

Zimmerman JA, Trombetta LD, Carter TH, Weisbroth SH
Dept. Biological Sciences, St. John's Univ., Jamaica, NY, 11439
Gerontology; 28(2):114-120 1982

We have studied the ability of N-methyl-N'-nitrosourea to induce pancreatic carcinoma within 5 mo when single doses were administered to C57BL/6J male mice at 3, 12 and 24 mo of age. Pancreatic tumors were not observed in the young and middle-aged animals, but 3/15 of the surviving aged mice showed gross evidence of carcinoma. Ultrastructural analysis revealed in each tumor the presence of two populations of undifferentiated cells, both cell types possibly being of acinar cell origin. The observation of pancreatic carcinoma only in aged animals treated with an environmental carcinogen may be a model paralleling the human condition, which also shows a strong age dependency. (Author abstract) (25 Refs)

REVIEWS AND OTHER RELATED STUDIES

59. EXPERIMENTAL COLORECTAL CARCINOGENESIS.

Martin MS
Laboratoire d'Immunologie, Faculte de Medecine, 7, boulevard Janne-d'Arc, F-21033 Dijon, France
Gastroenterol Clin Biol; 6(4):382-391 1982

Multiple intestinal tumors have successfully been induced in rats following 6 mo of subcutaneous injection with 1,2-dimethylhydrazine (DMH). The specificity of DMH depends to a large extent on the mode of administration, and the dose modifies the distribution of the lesions. DHM induces more intestinal tumors at low doses than some of the other compounds used for carcinogenic purposes. Age of the animal has an effect on the specificity of the action of carcinogens. Sex of the animal is also a factor in intestinal carcinogenesis. Intestinal tumors induced by DMH appear more rapidly in males than in females who seem less susceptible to colorectal cancers. The most frequently induced tumors are adenocarcinomas which occurs most often in the distal half of the colon. Mucous secreting carcinomas which predominate in the proximal part of the colon are less commonly encountered. Adenomas are observed much more commonly in the mouse than in the rat and they resemble the human adenomas. Like human colon cancers, experimental cancers of the colon can produce more or less specific antigens. The morphological transformation of the colons epithelial cells is accompanied by biochemical alterations and complex interactions affecting nutrition, intestinal flora, biliary acids, and immune defenses. Animal models are necessary to study the complicated assortment of factors in human colon cancer. (107 Refs) (In FRE)

60. EARLY PROLIFERATIVE CHANGES IN GASTROINTESTINAL NEOPLASIA.

Deschner EE
Lab., Digestive Tract Carcinogenesis, Memorial Sloan Cancer Center, 1275 York Ave., New York, NY, 10021
Am J Gastroenterol; 77(4):207-211 1982

The proliferative behavior of mucosal epithelium is reviewed in relation to the development of gastrointestinal cancer. An enlarged proliferative compartment has been recognized among individuals with a previous history of colon cancer, those with an isolated polyp, asymptomatic relatives of familial polyposis patients, those with ulcerative colitis, and even some members of the general population. Mucosa of patients with a previous history of colon cancer may show both extension of the proliferative compartment to the luminal surface (Stage I defect) and a shift in the major zone of DNA synthesis from the lower third of the gland to the middle and upper portion of the crypt (Stage II defect). Studies of 1,2-dimethylhydrazine-induced colon carcinogenesis in mice indicate that Stage II abnormalities are predictive of the development of cancer. Distribution of DNA synthesizing cells among patients belonging to several high risk groups is presented. Only 30% of the patients showed a completely normal proliferative pattern. Changes in proliferative patterns over time are described for two asymptomatic members of polyposis coli families. Histologically normal mucosa from patients with a previous history of neoplasia may show crypts with extremely elevated labeling indices. The importance of such crypts is discussed. Correlation of an abnormal proliferative pattern with the type of tumor that will emerge is described. The impact of a diet rich in animal and dairy fats is considered. (16 Refs)

61. GASTRIC CANCER.

Welch CE
Boston, MA
Prensa Med Argent; 68(17):723-726 1981

Gastric cancer was reviewed with reference to incidence (geographic differences, decrease, diet, meat, and nitrites), early diagnosis, mortality, gastric ulcer, gastric polyposis, pernicious anemia, giant hypertrophic gastritis, diagnosis (radiographic, endoscopic, cytologic, and exploratory laparoscopic), different malignant gastric lesions, surgical treatment (location, staging, metastases, lymph nodes, and drainage), survival, and adjuvant therapy (chemotherapy and radiotherapy). (no Refs) (In SPA)

62. HEREDITARY ADENOMATOSIS OF THE COLON AND RECTUM: RELEVANCE TO CANCER PROMOTION AND CANCER CONTROL IN HUMANS.

Kopelovich L
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Cancer Genet Cytogenet; 5(4):333-351 1982

Means of detecting persons at risk for colorectal cancers are described. SF cells, derived from normal-appearing biopsies of ACR gene carriers, appear to exist in an initiated state as the result of a dominant mutation. Topics discussed in relation to ACR and SF cells and colorectal neoplasms include the following: membrane-associated parameters, metabolic alterations, differential susceptiblity to transformation by chemical and physical agents and oncogenic viruses, cancer-related antigens, tissue culture studies, tumor promotion, genetic mechanisms, and cancer prognosis and control. (141 Refs)

63. GENETIC INFLUENCES IN HUMAN TUMORS.

Knudson AG
Graduate Sch. Biomedical Sciences, Univ. Texas Health Science Center, Houston, TX
Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.

Genetic states predisposing to cancer include chromosomal disorders such as Down's syndrome and Klinefelter's syndrome with increased risks of leukemia. The syndromes of Fanconi and Bloom are both autosomal recessive disorders which predispose to leukemia and cancer. Ataxia-telangiectasia is another autosomal recessive disease associated with chromosomal abnormality and a strong predisposition to lymphoid neoplasia. Xeroderma pigmentosum is a genetic state which predisposes to environmentally induced skin cancer. Dominantly inherited tumors differ sharply from the genetic conditions previously discussed in that tumor is a critical phenotypic feature and occurs with high penetrance. In some instances, a tumor is part of a syndrome, other manifestations of which are other kinds of tumors or nonneoplastic signs. In other instances tumor occurs in just one tissue, although it may be multiple in that tissue. Tumor syndromes include polyposis of the colon, Gardner's syndrome, hereditary adenocarcinomatosis, basal cell nevus syndrome, multiple endocrine tumor syndromes, neurofibromatosis, von Hippel-Lindau syndrome and tuberous sclerosis. Specific tumors which are inherited but not part of a syndrome are retinoblastoma, Wilms' tumor of the kidney and neuroblastoma. (57 Refs)

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NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. MICROWAVE HEATING ENHANCES THE MIGRATION OF PLASTICIZERS OUT OF PLASTICS.
Bishop CS, Dye A
East Tennessee State Univ., Johnson City, TN, 37614
J Environ Health; 44(5):231-235 1982

2. DISEASES CAUSED BY EPOXY RESINS.
Konietzko H, Fischer G
Institut fur Arbeits- und Sozialmedizin, Johannes-Gutenberg-Universitat, Obere Zahlbacher Strasse 67, D-6500 Mainz, W. Germany
Zentralbl Arbeitsmed Arbeitsschutz Proph; 32(3):86-91 1982
In GER

3. NITROSAMINES.
Aigner K
Pneumonologische Abteilung, Krankenhaus der Elisabethinen, Fadingerstr. 1, A-4020 Linz-Donau, Austria
Wien Med Wochenschr; 132(71,Suppl):75-79 1982
In GER

4. EXPERIMENTAL TUMORS OF THE PERIPHERAL NERVOUS SYSTEM.
Beniashvili DS
Cancer Res. Center, Tbilisi, USSR
Eksp Onkol; 4(2):12-19 1982
In RUS

5. MUTAGENIC, CARCINOGENIC AND TERATOGENIC EFFECTS OF STYRENE.
Sram RJ, Pohlova H, Topinkova E
Klinika hygieny a epidemiologie, Srobarova 48, 100 42 Prague 10, Czechoslovakia
Prac Lek; 34(2):68-72 1982
In CZE

6. DIETHYLSTILBESTROL: EFFECT OF IN UTERO EXPOSURE.
Burke L
Obstetrics/Gynecology Dept., Harvard Medical Sch., Boston, MA
Curr Probl Obstet Gynecol; 5(2):1-58 1981

7. IN UTERO EXPOSURE TO DIETHYLSTILBESTROL: ADVERSE EFFECTS ON THE REPRODUCTIVE TRACT AND REPRODUCTIVE PERFORMANCE IN MALE AND FEMALE OFFSPRING.
Stillman RJ
Dept. Obstetrics and Gynecology, George Washington Univ. Sch. Medicine and Health Sciences, 2150 Pennsylvania Ave., NW, Washington, DC, 20037
Am J Obstet Gynecol; 142(7):905-921 1982

8. BIOLOGICAL EFFECTS OF MINERAL WOOL.
Petersen R, Ehrhorn H, Mossing K, Sabroe S, Silberschmid M, Venstrup-Nielsen SE
Socialmedicinsk institut, Vesterbro Torv 1-3, DK-8000 Arhus C, Denmark
Ugeskr Laeger; 144(13):971-975 1982
In DAN

DIETARY FACTORS IN CARCINOGENESIS

9. NATURALLY OCCURRING FOOD TOXICANTS: PHENOLIC SUBSTANCES OF PLANT ORIGIN COMMON IN FOODS.
Singleton VL
Dept. Viticulture and Enology, Univ. California, Davis, CA
Adv Food Res; 27:149-242 1981

10. MUTAGENS, CARCINOGENS, AND TUMOR PROMOTERS IN OUR DAILY FOOD.
Sugimura T
Natl. Cancer Res. Inst., Tsukiji, Chuo-ku, Tokyo, Japan
Cancer; 49(10):1970-1984 1982

11. THE BIOLOGICAL EFFECTS OF CARRAGEENAN AND OTHER SULFATED POLYSACCHARIDES WITH PARTICULAR ATTENTION TO IMMUNOLOGICAL AND CARCINOGENIC PROPERTIES.
Larsen B
Kraeftforskningsinstituttet, DK-8000 Arhus C, Denmark
Ugeskr Laeger; 144(12):860-863 1982
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Vopr Onkol; 28(2):3-9 1982
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Dept. Environmental Health, Univ. Washington, Seattle, WA, 98195
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In RUS

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Richardson BJ, Waid JS
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Search; 13(1/2):17-25 1982

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Pathobiol Annu; 11:1-29 1981

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Zentralinstitut fur Krebsforschung, Akademie der Wissenschaften der DDR, Lindenberger Weg 80, DDR-1115 Berlin-Buch, E. Germany
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In GER

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Dept. Veterinary Science, Coll. Agricultural and Life Sciences, Univ. Wisconsin, 1655 Linden Drive, Madison, WI, 53706
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Excerpta Med Int Congr Ser; 576:1-16 1981

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Rowe WP
Lab. Viral Diseases, Natl. Inst. Allergy and Infectious Diseases, NIH, Bethesda, MD, 20205
Cancer; 49(10):1958-1962 1982

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Weiss RA
Chester Beatty Res. Inst., Fulham Road, London SW3 6JB, England
Symp Soc Gen Microbiol; 33:267-288 1982

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Symp Soc Gen Microbiol; 33:227-247 1982

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Seemayer TA, Oligny LL, Gartner JG
Dept. Pathology, Montreal Children's Hosp., Montreal, Quebec, Canada
Perspect Pediatr Pathol; 6:1-33 1981

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Groopman JE, Gottlieb MS
Div. Hematology-Oncology, Univ. California at Los Angeles Sch. Medicine, Los Angeles, CA
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Pliss GB, Turusov VS, Zabezhinskii MA
No affiliation given
Vopr Onkol; 28(2):18-22 1982
In RUS

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Pol Tyg Lek; 37(2):63-67 1982
In POL

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DeVita VT, Hellman S, Rosenberg SA

NCI, Bethesda, MD
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Cold Spring Harbor Lab., Box 100, Cold Spring Harbor, NY, 11724
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PREVALENCE OF GI CANCER IN HUMAN POPULATIONS

1. A STUDY OF THE DEATH RATE IN JAPAN BASED ON CAUSE AND SOCIAL ENVIRONMENT - APPLICATION OF MULTIVARIATE STATISTICAL ANALYSIS.

Iwamoto M, Dodo H, Yoneda J, Ueda Y
Dept. Hygiene, Yamaguchi Univ. Sch. Medicine, Ube, Japan
Nippon Eiseigaku Zasshi; 36(4):678-686 1981

A varimax rotation was applied to statistical data collected during 1970 and 1975 in all 46 prefectures in Japan after performing a principal component analysis of 12 major causes of death and 7 sociogeographical conditions. The 12 major causes of death included malignant neoplasms, stomach cancer, cerebrovascular disease, lung cancer, heart disease, pneumonia and bronchitis, and the environmental conditions included primary industrial rate, mean temperature, water and sewer diffusion rates. Three principal factors were arrived at by factor analysis and varimax rotation. The first factor explained 29.26% of the total variance observed in the causes of death due to urbanization. That is to say, the major causes of death in urban areas was lung cancer and gastric cancer and that in rural areas was

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accidents. The second factor explained disease patterns related to temperature. That is, major causes of death were liver cirrhosis, tuberculosis, and hypertension in western Japan and were stomach cancer and cardiovascular disease in eastern Japan. The third factor explained characteristics associated with the disease patterns in northern agricultural areas of Japan. (11 Refs) (In JPN)

2. SOCIO-ECONOMIC CLASS DIFFERENCES IN CANCER INCIDENCE IN CALI, COLOMBIA.

Cuello C, Correa P, Haenszel W
Dept. Pathology, Faculty Medicine, Universidad del Valle Cali, Cali, Colombia
Int J Cancer; 29(6):637-643 1982

Based on census tract information, cancer incidence rates for three socioeconomic strata of the city of Cali, Colombia, were calculated. Strong negative associations with socioeconomic status were found for cancers of the cervix and stomach. Colon cancer and endocrine-related cancers were positively associated with socioeconomic status, while no such association was found for rectal cancer. Contrary to data from developed countries, all smoking-related cancers were positively associated with socioeconomic class. The role of socio-economic gradients in developing countries is stressed as a basis for etiological research. (Author abstract) (30 Refs)

3. GASTRIC CARCINOMA IN A TROPICAL AFRICAN POPULATION.

Ajao OG
Dept. Surgery, Univ. Ibadan, Ibadan, Nigeria
East Afr Med J; 59(1):70-75 1982

Types of gastric carcinoma, either intestinal or diffuse, found in the tropical African population based on Lauren's classification were studied in 90 patients (55 males, 35 females, 23-73 yr old) with gastric neoplasms. The highest incidence (32.2%) occurred in patients greater than 70 yr old and (28.9%) in those greater than 60 yr old. Of the 90 patients observed, only 56 had full investigations and all the necessary data fully documented. All the patients presented with epigastric pain, wt loss, weakness, fullness after a small meal, and occasional vomiting, especially after meals. Most of the lesions (89.7%) were in the gastric antrum, 5.1% in the body, 5.1% in the fundus, and none was found in the cardiac portion. (13 Refs)

4. CANCER AMONG BLACKS IN NEWARK, NEW JERSEY, 1970-1976. A NATIONAL AND INTERNATIONAL COMPARISON.

Thind IS, Najem R, Paradiso J, Fuerman M
Dept. Preventive Medicine and Community Health, New Jersey Medical Sch., Coll. Medicine and Dentistry, 100 Bergen St., Newark, NJ, 07103
Cancer; 50(1):180-186 1982

Newark black men had age-adjusted cancer rates comparable to those of Washington, DC, but lower than the other three American city blacks. Rates for Newark black women were generally similar to other American black women. American blacks, like those of Newark, had cancer rates higher than the African blacks in three out of four countries studied. Only blacks of Rhodesia had cancer experience like that of American blacks. Except for cancer of the cervix, the African blacks had generally lower rates compared to the American blacks for the 10 sites investigated. However, high rates did occur for certain sites, eg, esophagus and bladder cancers in Bulawayo, Rhodesia. Newark blacks also had higher rates for certain sites (prostate, lung, breast and cervix) compared to Washington, DC, and certain other US cities. Thus, the total risk of malignancies to develop among Newark blacks was no greater than that expected, based upon the four US cities' experience. (Author abstract) (39 Refs)

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN GI CARCINOGENESIS

5. MORTALITY RISKS IN AUSTRALIAN MEN BY OCCUPATIONAL GROUPS, 1968-1978. VARIATIONS ASSOCIATED WITH DIFFERENCES IN DRINKING AND SMOKING HABITS.

McMichael AJ, Hartshorne JM

Div. Human Nutrition, Commonwealth Scientific and Industrial Res. Organization, Kintore Ave., Adelaide 5000, Australia

Med J Aust; 1(6):253-256 1982

Analysis of patterns of male mortality in Australia during 1968-1978 shows elevated death rates for liver cirrhosis, alcoholism and alcoholic psychosis in various rural, service, and 'blue-collar' occupations. The risks of mortality from lung cancer and cancers of the upper alimentary tract and larynx - sites influenced by alcohol and tobacco consumption - are raised in the latter two groups. In contrast, the risks of mortality from cancer of the colon, thought to be influenced by dietary 'affluence', are consistently higher for professional and 'white-collar' groups. As reported in other populations, stomach cancer mortality risks are higher for service and blue-collar groups. The risks of mortality from coronary heart disease and cerebrovascular disease are also higher, albeit moderately, for these two groups. The consideration of personal behavior as a reflection of socioeconomic and subcultural influences is a prerequisite to effective community health education. (Author abstract) (20 Refs)

6. RELATIONSHIP OF SITE-SPECIFIC CANCER MORTALITY RATES TO ALTITUDE.

Amsel J, Waterbor JW, Oler J, Rosenwaike I, Marshall K

Sch. Medicine, Program Epidemiologic Res. and Training, Univ. Pennsylvania, Nursing Education Building, 420 Service Drive S2, Philadelphia, PA, 19104

Carcinogenesis; 3(5):461-465 1982

Mortality rates for all malignant neoplasms (combined) and for 34 site-specific cancer categories for selected high and low altitude populations are compared using two related techniques: confidence interval overlap for strictly descriptive purposes and analysis of standardized mortality ratios using lower and upper 95% statistical significance factors for the ratio of an observed value of a Poisson variable to its expectation. Techniques are employed to minimize confounding due to industrialization, urbanization or selected cultural characteristics. Cancer mortality data for US counties averaged over the 20-yr period, 1950-1969, were used. For most comparisons a deficit in cancer mortality in high altitude counties was observed. The largest differences between the low and high altitude groups were found for cancers of the tongue and mouth, esophagus, larynx, lung and melanoma. Some limitations of ecologic studies are discussed. (Author abstract) (18 Refs)

7. CANCER MORBIDITY AMONG POLISHERS.

Jarvholm B, Thiringer G, Axelson O
Dept. Occupational Medicine, Sahlgrenska sjukhuset, Gothenburg, Sweden
Br J Ind Med; 39(2):196-197 1982

The mortality pattern among 86 men was determined to investigate the possible hazards of polishing steel. The men had polished steel with polishing paste for at least 5 yr. The polishing pastes had contained tallow, beeswax, carnauba wax, alundum, carborundum, ferric oxide, and chalk. A total of 18 men had died compared with 13.3 expected. Four had died of stomach cancer compared with 0.44 expected (less than 0.005). The mortality for other causes of death was not increased. The study does not permit any definite conclusion but indicates a possible cancer hazard among polishers. (Author abstract) (8 Refs)

8. DEVELOPMENT, LIFE STYLES AND ONCOGENIC HAZARDS.

Ramalingaswami V
Indian Natl. Science Acad., Delhi, India
Indian J Cancer; 19(2):65-70 1982

Variations in incidence of some cancers in different societies indicate that there are important environmental factors in their causation, such as cancers of the uterine cervix and esophagus in Asia. Factors such as tobacco smoking, community participation, industrialization, and investigation of epidemics due to unusual circumstances (aflatoxin poisoning) are discussed. Developing countries carry a double burden of poor health conditions while at the same time developing new health problems due to industrialization. (15 Refs)

9. INFLUENCE OF NITRATES ON THE HEALTH STATUS OF THE POPULATION.

Vondrakova M
Institut hygieny a epidemiologie, Srobarova 48, 100 42 Prague 10, Czechoslovakia
Cesk Hyg; 27(3):162-172 1982

Studies on the health effects of nitrates and nitrites are reviewed. Nitrates and nitrites possibly participate in the formation of carcinogenic N-nitroso compounds (N-nitrosodimethylamine, N-nitrosodiethylamine, N-nitrosopyrrolidone and N-nitrosopiperidine) in foods and organisms. Recent epidemiological studies show a correlation between the incidence of carcinoma of certain localizations (especially of the stomach) and the presence of nitrosamines, nitrates and nitrites in the environment. (80 Refs) (In CZE)

DIETARY AND DIGESTIVE FACTORS IN GI CARCINOGENESIS

10. THE ROLE OF DIETARY FIBER IN LIPID METABOLISM.

Story JA
Dept. Foods and Nutrition, Purdue Univ., West Lafayette, IN
Adv Lipid Res; 18:229-246 1981

The interaction of dietary fiber in lipid metabolism and in lipid-associated disease is discussed. In spite of strong relationships indicated by epidemiological studies, little is known concerning the mechanisms involved and details concerning specific types of dietary fibers involved. The magnitude of the interaction between some types of dietary fiber and bile acids appears sufficient to result in an alteration of bile acid excretion and, as a result, alter sterol balance. At the same time, a resultant increase in concentration of bile acids in the colon may be related to susceptibility to colon carcinogenesis. In one experimental study, the feeding of three types of dietary fiber (alfalfa, cellulose, or bran) led to significantly reduced colon tumors induced by azoxymethane (AOM) when dietary fat was reduced from 35% to 7%. Another study involving use of AOM and intrarectal instillation of methylnitrosourea and various dietary fibers indicated that those fibers which result in dilution of bile acids (eg, bran, cellulose) result in the most consistent reduction in chemically induced colon tumors. (67 Refs)

11. MUTAGENS IN HUMAN FAECES. ARE THEY RELEVANT TO CANCER OF THE LARGE BOWEL?

Venitt S
Chester Beatty Res. Inst., Nightingales Lane, Chalfont St. Giles, Bucks HP8 4SP, England
Mutat Res; 98(3):265-286 1982

Bacterial mutation studies and cytogenetic studies of extracts of human feces (HF) and the role of mutagens in HF are reviewed. The hypothesis that colorectal cancer might be caused by carcinogenic chemicals generated endogenously by metabolism of fecal substrates by the gut microflora has been tested directly, using short-term assays which have been developed for detecting potential carcinogens. Studies on nitrate, nitrite, and nitrosamines in the intestinal tract (IT) showed that conditions in the lower IT favor denitrification rather than nitrification. Bacterial mutagens have been detected in fecal extracts obtained from several groups of subjects drawn from widely differing communities and consuming very different diets. Chromosome-damaging activity has also been demonstrated in extracts of HF, this latter finding being based on a very small sample group. Therefore, studies indicate that normal people regularly excrete feces which contains constituents possessing properties (mutagenicity and clastogenicity) characteristic of carcinogens. The possibility that the mutagenic activity of fecal extracts is artefactual cannot be excluded until extraction and mutagenesis assays are preformed under anaerobic conditions. Apart from the metabolic activity of fecal flora occupying the colonic lumen, the colonic epithelium itself possesses enzyme systems capable of metabolizing xenobiotics to mutagenic derivatives. The complex interaction between dietary fiber, transit time, and the frequency of bowel movements must also play a part in modifying the response of the colonic epithelium to continuous assaults by fecal mutagens. The protective mechanisms would operate within certain upper limits, which, if exceeded, would be expected to allow reversible or irreversible damage to occur to molecular and cellular components of the mucosa. (58 Refs)

12. DIETARY FIBER AND CANCER.

Kritchevsky D, Story JA
Wistar Inst. Anatomy and Biology, Philadelphia, PA
Advances in Human Clinical Nutrition. Vitale JJand Broitman SA, ed. Littleton, MA, John Wright - PSG Inc., 217 pp., 1982.

The role of dietary fiber in the development of cancer of the large bowel is discussed. Mechanisms by which a high-fiber diet may protect against colon cancer may involve bile acid metabolism, production of volatile fatty acids through the interaction of intestinal flora with fiber, steroid metabolism, and carcinogens. It is noted that in general, populations ingesting diets high in fiber, do not eat a Western diet. (24 Refs)

13. ON THE RELATIONSHIP BETWEEN NUTRITION AND THE DEVELOPMENT OF TUMORS.

Kolb E
Wissenschaftsbereich Tierbiochemie, Karl-Marx-Universitat Leipzig, Semmelweisstrasse 4, DDR-7010 Leipzig, E. Germany
Z Gesamte Inn Med; 37(6):169-176 1982

Chronic intake of carcinogens and cocarcinogens in the diet is a primary factor in the development of tumors in humans. High intake of meats has been linked to cancers of the colon and breast. Reduction in intake of animal fats to less than 50 g/day and increase in intake of raw fibers and carotenes are recommended. Small amounts of smoked meat and fish are not considered to be harmful. Foods containing aflatoxins from fungi should be avoided. (50 Refs) (In GER)

14. EPIDEMIOLOGICAL FINDINGS ON ESOPHAGEAL CANCER IN THE VENETO REGION.

Rossi M, Ancona E, Mastrangelo G, Solimbergo D, Paruzzolo P, Azzarini G, Sorrentio P, Peracchia A
Clinica Chirurgica III, Universita di Padova, Padova, Italy
Minerva Med; 73(22):1531-1540 1982

A study of 150 patients (125 men, 25 women, 40-71 yr old, av age 57.9 yr) with esophageal cancer and 150 control individuals (125 men, 25 women) is reported. Based on their daily and total consumption of tobacco, alcohol and corn flour the patients were categorized into relative risk groups. It was found that a daily alcohol consumption of 81 g/day or higher and a corn flour consumption in excess of 36 g/day significantly increased the relative risk factor (Rf). Tobacco use had no significant influence on the Rf. Combinations of more than one risk factor (alcohol, tobacco, corn flour) did not have a synergetic but a merely additive effect. Alcohol use was directly correlated to the incidence of esophageal cancer in 11.64% of cases, and corn flour use was correlated to cancer etiology in 3.96% of the patients. However no significant correlation could be established in 84.4% of the cases and causative factors remained unknown. It is suggested that other risk factors may have been related to general nutrition and vitamin and mineral intake. (44 Refs) (In ITA)

15. SUMMARY OF A WORKSHOP ON CHOLESTEROL AND NONCARDIOVASCULAR DISEASE MORTALITY.

Feinleib M
Div. Heart and Vascular Diseases, Natl. Heart, Lung, and Blood Inst., Bethesda, MD, 20205
Prev Med; 11(3):360-367 1982

Data from 17 population studies concerning the question of whether very low cholesterol levels (usually below 180 mg/deciliter), while favorably affecting mortality rates from coronary heart disease, might be related to excess incidence and deaths from other causes including cancer were reviewed. Inconsistent relationships between cholesterol concentration and mortality from noncardiovascular disease and malignant neoplasms were found. Eight studies found an inverse relationship between serum cholesterol and mortality from malignant neoplasms in men; none found a significant association between these variables in women. Four studies found a significant inverse association between blood cholesterol and colon cancer in men; similar but not significant associations were seen in two other studies. No other specific sites of cancer exhibited a significant association in more than one or two studies. While the data did not substantiate any direct cause-and-effect relationship between low blood cholesterol and cancer, low blood cholesterol could possibly be a genetic 'marker' for a small number of cancer-prone males in a given population. No pathogenetic mechanism could be supported with the data reviewed. The current public health message recommending limitation of cholesterol intake by those with elevated cholesterol levels should not be changed based on the data reviewed, and physicians should continue to advise reduction of blood cholesterol levels for all persons exhibiting higher than normal levels. (13 Refs)

16. NITRATE IN DRINKING WATER AND CANCER IN NORTHERN JUTLAND, DENMARK, WITH SPECIAL REFERENCE TO STOMACH CANCER.

Jensen OM
Danish Cancer Registry, Strandboulevarden 49, DK-2100 Copenhagen 0, Denmark
Ecotoxicol Environ Saf; 6(3):258-267 1982

Cancer risk in an area with long-term evidence of nitrate in drinking water was studied, and cancer morbidity was compared with that in neighboring towns with zero or low levels of nitrates in water, and in Danish provincial towns. A slight but significant increased risk of developing cancer of the stomach was found in Aalborg compared to neighboring towns and provincial towns; the increase was consistent over the period 1943-1976. A decrease in stomach cancer was noted in all places studied over the period examined. (33 Refs)

17. MUTAGENICITY OF HYDROLYSATES OF CITRUS FRUIT JUICES.

Mazaki M, Ishii T, Uyeta M
Public Health Inst. Kochi Prefecture, 2-4-1, Marunouchi, Kochi 780, Japan
Mutat Res; 101(4):283-291 1982

Hydrolysates of citrus fruit juices obtained with acid, enzymes, and human intestinal bacteria were tested for mutagenicity in the Ames test using strains TA98 and TA100. The hydrolysates of all citrus fruit juic canned orange juice, fresh fruit juice of mandarin orange, grapefruit, navel orange, 'Ponkan', and pomelo used in the study were mutagenic. Mutagenicities were found in both the chloroform extract and the ether extract. The chloroform extracts were mutagenic to TA98 and TA100 with S9 mix, and the ether extracts were mutagenic to TA98 and TA100 with or without S9 mix. (19 Refs)

OTHER ETIOLOGIC FACTORS IN GI CARCINOGENESIS

18. REMNANT GASTRIC CANCER AND ITS PRECANCEROUS LESIONS: JAPANESE PREVALENCE AND HISTOLOGICAL FEATURES ASSOCIATED WITH POST-OPERATIVE CHRONOLOGICAL YEAR (MEETING ABSTRACT).

Umeda N, Matsueda K, Shimojo E, Sakagami R, Takazoe M, Oami H
National Medical Center Hospital, Tokyo, Japan
Gastroenterology; 82(5,part2):1201 1982

The remnant stomach (RS) may have constant mucosal damage because of regurgitation of intestinal juice. This may play important roles in the development of remnant gastric cancer (RGC) and its locational distribution. Sixteen cases of RGC in our institution were studied and their chronological prevalence, location and morphological features were investigated. Another 55 cases of RS without cancer were also examined by endoscopic biopsies to evaluate their dysplastic changes. Furthermore, 279 cases of reported RGC in Japan were reviewed and the similar studies were carried out. Morphological analysis of our 16 cases showed 2 early gastric cancers (IIc,IIa+IIc) and 13 advanced gastric cancers (Borrmann-Type2:3, Type3:9, Type4:1). Their average age was 65.1 yrs and post-operative chronological year (POCY) for developing RGC was average 21.5 yrs (13-41 yrs). The most common location of RGC was at and around the stoma (63%) and the most common operative method associated with RGC was Billroth II (B-II) anastomosis. The similar results were also seen among the 279 cases of reported RGC in Japan. Increasing severity of mucosal dysplasia would likely develop if the POCY was more than 10 yrs, and this trend was especially true in B-II anastomosis. (no Refs)

19. COMPLICATIONS OF PEPTIC ULCER IN 651 CASES.

Zhao H, Ren L, Pu Z, Su J
Dept. Internal Medicine, Second Affiliated Hosp., Lanzhou Medical Coll., Lanzhou, People's Republic of China
Zhonghua Xiaohua Zazhi; 1(3):206-207 1981

Clinical findings are described for 333 cases of gastric ulcer, 282 cases of duodenal ulcer and 36 cases of multiple-type ulcer. There were 537 males and 114 females, 7 to 82 yr old. Complications included upper gastrointestinal bleeding (49.46%), pyloric stenosis (14.59%) and cancerous changes (0.92%). Among the cancerous patients, all had history of ulcer for 4 to 20 yr; histological types included gastric adenocarcinoma (3 cases), mucinous carcinoma (2 cases) and simple carcinoma (1 case). (8 Refs) (In CHI)

20. THE OCCURRENCE OF GASTRIC STUMP CANCER IN A US POPULATION (MEETING ABSTRACT).

Hiltz SW
Division of Gastroenterology, Henry Ford Hospital, Detroit, MI, Schuman, B. M.
Gastrointest Endosc; 28(2):133 1982

Many reports from European countries with a rate of gastric cancer three times that of the US have shown an increased risk of gastric cancer 10 to 15 years after gastric resection for benign disease. We undertook a combined retrospective chart review of patients who had undergone partial gastrectomy prior to 1960 and a prospective evaluation of patients (regardless of symptoms) presenting to our clinic with a history of a subtotal gastrectomy ten or more years prior. Also symptomatic patients with more recent surgery were studied. The 66 patients who either underwent endoscopy as part of the prospective study or were found on chart review to have had a recent endoscopy had an average follow-up of 22.2 years. There were 4 cases with cancer of the gastric stump, 3 cases with atypia and 7 cases with gastric polyps, 6 of which were adenomatous. The maximum expected rate of adenocarcinoma of the stomach in the US is 0.85% in 20 years for a population 50 years old. This study of US patients confirms the increased rate of gastric cancer following subtotal gastrectomy reported from Europe. In fact, the rate in the patients followed with endoscopy (6.1%) matches endoscopic series reported abroad. (no Refs)

21. MUTAGENS PRODUCED BY THE PYROLYSIS OF OPIUM AND ITS ALKALOIDS AS POSSIBLE RISK FACTORS IN CANCER OF THE BLADDER AND OESOPHAGUS.

Malaveille C, Friesen M, Camus AM, Garren L, Hautefeuille A, Bereziat JC, Ghadirian P, Day NE, Bartsch H
(c/o Bartsch) Div. Environmental Carcinogenesis, International Agency Res. on Cancer, 150 cours Albert-Thomas, 69372 Lyon, Cedex 8, France
Carcinogenesis; 3(5):577-585 1982

Samples of opium pipe scrapings (opium dross, called sukhteh locally), but not of crude opium, collected in an area with a high incidence of esophageal cancer in north-east Iran, were shown to contain pro-mutagens, producing mostly frameshift mutations in Salmonella typhimurium strains TA1538 and TA98 after metabolic activation. Pyrolysis of opium and of its major alkaloid, morphine, yielded smoke condensates with mutagenic activities 10 and 100x higher, respectively, than that of the sukhteh samples tested. Heterocyclic aromatic hydrocarbons and primary aromatic amines present at different concentrations in these three pyrolysates are considered to be the major active principles. Opium addiction has been implicated as a risk factor in bladder cancer in humans and the ingestion of opium pyrolysates, in conjunction with dietary deficiencies, may be related to the high incidence of esophageal cancer in north-east Iran, although causality has not been established. (Author abstract) (29 Refs)

22. DISSEMINATED KAPOSI'S SARCOMA IN HOMOSEXUAL MEN.

Friedman-Kien AE, Laubenstein LJ, Rubinstein P, Buimovici-Klein E, Marmor M, Stahl R, Spigland I, Kim KS, Zolla-Pazner S
New York Univ. Medical Center, 530 First Ave., New York, NY, 10016
Ann Intern Med; 96(6,part1):693-700 1982

Nineteen cases from an epidemic of disseminated Kaposi's sarcoma in homosexual men were studied by clinical, virologic, immunologic, and genetic methods. The patients were all male homosexuals ranging in age from 29 to 52 yr, with histories of multiple sexually transmitted diseases and exposure to both prescription and recreational drugs. Sites of disease included skin (16 of 19 patients), lymph nodes (13 patients), gastrointestinal tract (12 patients), spleen (3 patients), and lung (1 patient). Most patients had elevated levels of serum immunoglobins, positive antibody titers to hepatitis A and B virus, cytomegalovirus and Epstein-Barr virus, and impairment of cell-mediated immunologic reactions. The frequency of HLA-DR5 in these patients was significantly elevated. Two of the 19 patients died. Although the precise cause of this epidemic is unknown, it is likely that a genetic predisposition, an acquired immunoregulatory defect, and one or more infectious agents and drugs may be involved. (Author abstract) (48 Refs)

23. GENETIC/EPIDEMIOLOGICAL FINDINGS IN A STUDY OF SMOKING-ASSOCIATED TUMORS.

Lynch HT, Fain PR, Albano WA, Ruma T, Black L, Lynch J, Shonka M
Dept. Preventive Medicine and Health, Creighton Univ. Sch. Medicine, 2500 California Street, Omaha, NB, 68178
Cancer Genet Cytogenet; 6(2):163-169 1982

While the etiology of bronchogenic carcinoma remains enigmatic, an expanding array of carcinogenic pollutants in interaction with host susceptibility factors has been implicated. We have studied family histories of cancer in a consecutive series of cancer patients from two university oncology clinics in Nebraska. Particular attention has been given to carcinoma of the lung and other putative smoking-associated cancers (oral cavity, esophagus, urinary bladder, pancreas). Smoking histories were obtained for relatives of an overlapping series of patients with these tumor sites. Findings revealed that, although a significant cohort effect was observed with respect to smoking habits for both relatives of lung cancer probands and for relatives of probands with other smoking-associated tumors, a corresponding trend for lung cancer frequency was observed only for relatives of lung cancer probands. This result suggests the importance of host factors in combination with environmental exposures in determining lung risk. A cohort trend for lung cancer was also apparent among relatives of breast cancer probands, but not for relatives of colon cancer probands, suggesting the possibility of an intrinsic association between carcinomas of the breast and lung. We believe that further elucidation of host factor susceptibility in lung cancer may have important etiological and preventive implications. (Author abstract) (38 Refs)

INDUCTION OF GI CARCINOGENESIS IN ANIMALS

24. ILEOCECAL (PARACECAL) MALIGNANT LYMPHOMA--IMMUNOBLASTOMA--IN HOODED RATS.

Nemeth P, Schneider J, Warzok R
Korbontani Intezet, POTE, Szigeti u. 12, 7643 Pecs, Hungary
Morphol Igazsagugyi Orv Sz; 22(2):117-123 1982

Spontaneous and chemically induced ileocecal (paracecal) malignant lymphoma (immunoblastoma) was studied in inbred strain E hooded rats compared with untreated outbred Wistar rats. The spontaneous incidence of ileocecal immunoblastoma was found to be 5% in 95 untreated hooded rats, and the tumors were detected between days 545 and 740 of life. The spontaneous incidence was found to be 0% among more than 400 untreated Wistar rats of two different strains. The immunoblastoma incidence was found to be 8-41% among hooded rats treated prenatally or postnatally with the combinations of ethylurea (0.5%), methylurea (0.2-0.3%), isopropylurea (0.4%), n-propylurea (0.4%), butylurea (0.4%) in drinking water or ephedrine (0.5% in feed) or Obesin (40 mg/kg) with sodium nitrite (0.2-0.5% in feed or 40 mg/kg 12 times every 2 wk through gastric probe). The incidence was found to be highest in the group treated with the combination of 0.4% propylurea and 0.3% sodium nitrite postnatally and lowest in that treated with 0.4% isopropylurea and 0.3% sodium nitrite postnatally. The tumors were detected in the treated animals between days 194 and 789 of life. The induced tumors were identified histologically as transfollicular immunoblastomas, showing no difference from the spontaneous ones. The tumor incidence was increased and the latent period shortened by treatment with the N-nitroso compounds. (22 Refs) (In HUN)

25. NEW CONSIDERATIONS ON HYDROGEN PEROXIDE AND RELATED SUBSTANCES AS FOOD ADDITIVES IN VIEW OF CARCINOGENICITY.

Ito R
Dept. Pharmacology, Toho Univ. Sch. Medicine, Tokyo, Japan
Paediatrician; 11(3/4):222-224 1982

The actions of potassium bromate (used as an improving agent in bread) and sodium chlorate (used as a weed killer) are under study because of the finding of hyperplasia in the duodenal mucosa of mice after long-term oral feeding with H2O2. Mutagenicity of bromate was shown in the Ames test but carcinogenicity is still under study. It has been ruled in Japan that H2O2 is safe for use in food when it is entirely decomposed. (3 Refs)

MECHANISMS AND MODIFICATIONS OF GI CARCINOGENESIS

26. SELENIUM AND THE ACUTE EFFECTS OF THE CARCINOGENS, 2-ACETYLAMINOFLUORENE AND METHYLAZOXYMETHANOL ACETATE.

Banner WP, Tan QH, Zedeck MS
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Cancer Res; 42(8):2985-2989 1982

Selenium inhibits the development of 2-acetylaminofluorene-induced hepatic tumors and methylazoxymethanol-induced colon tumors. It has been suggested that selenium exerts these protective effects by inhibiting metabolic activation of the carcinogen. We have studied the effects of selenium upon the acute inhibition of RNA and DNA synthesis induced by 2-acetylaminofluorene or methylazoxymethanol in intact liver, regenerating liver, and colon of weanling male Sprague-Dawley rats. Some animals received selenium in the drinking water (4 ppm) for 1 wk, while others received a single injection of selenium (1 mg/kg ip) prior to being treated with the carcinogens. No protection against the effects of the carcinogens on RNA or DNA synthesis was noted with either treatment of selenium. Disulfiram did protect against the 2-acetylaminofluorene-induced inhibition of hepatic RNA synthesis, and pyrazole prevented the inhibition of RNA synthesis induced by methylazoxymethanol in both liver and colon. Serum selenium levels are reported. The data indicate that selenium does not influence the acute alterations induced by the carcinogens 2-acetylaminofluorene or methylazoxymethanol and suggest that the tumor-preventive effects of selenium are probably due to a mechanism other than interference with carcinogen activation and interaction with cellular macromolecules. (Author abstract) (34 Refs)

27. EFFECT OF SELENIUM ON THE INDUCTION OF BREAST FIBROADENOMAS BY ADENOVIRUS TYPE 9 AND 1,2-DIMETHYLHYDRAZINE-INDUCED BOWEL CARCINOGENESIS IN RATS.

Ankerst J, Sjogren HO
Wallenberg Lab., Univ. Lund, Lund, Sweden
Int J Cancer; 29(6):707-710 1982

Selenium in its organic and inorganic forms has been shown to inhibit the development of chemically induced, spontaneous and transplanted tumors. The present investigation was performed to study the effect of selenium (4 ug per ml of drinking water) on tumorigenesis of adenovirus-type-9-induced breast fibroadenomas and on 1,2-dimethylhydrazine-induced bowel carcinogenesis in WF rats. It was found that identical treatment with Se under identical conditions and with no obvious toxic effects on the rats (1) resulted in inhibition of DMH-induced large-bowel carcinogenesis; (2) facilitated induction of small-bowel cancer by the same carcinogen in the same animals, and (3) greatly facilitated induction of breast fibroadenoma by adenovirus Type 9 in the same strain of rats. The effect of Se treatment on DMH-induced large-bowel carcinogenesis confirms previous findings and proves that the opposite effect on fibroadenoma development is not due to differences in eg effective dose, animal strains or condition of the animals. It is not yet clear through which mechanisms Se exerts these effects. (Author abstract) (29 Refs)

28. DIFLUOROMETHYLORNITHINE (DFMO) DIMINISHES 1,2-DIMETHYLHYDRAZINE-INDUCED (DMH) COLONIC CARCINOGENESIS IN MICE (MEETING ABSTRACT).

Kingsnorth AN, King WW, McCann PP, Diekema K, Ross JS, Malt RA
Department of Surgery, Harvard Medical School, Boston, MA, 02114
Gastroenterology; 82(5,part2):1100 1982

Effects of specific irreversible inhibition of ornithine decarboxylase (ODC) with DFMO were evaluated in view of evidence directly linking the intensity of cell proliferation to DMH-carcinogenesis. Male CDI mice (168) were injected weekly with DMH (20mg/kg) for 28 weeks with or without 1% DFMO in the drinking water. DFMO (mean intake 2.8g/kg/day) caused 93% inactivation of colonic ODC activity. Thirty minutes before death at 28 weeks all animals received an sc injection of 25 uCi [3H]methyl-thymidine. Full thickness specimens of colon were analyzed later for ODC, polyamines, DNA content, RNA content, DNA specific activity, crypt depth, and number of tumors. Throughout the 28 weeks of the experiment, DMH-treated mice had similar colonic ODC activity to controls. At 28 weeks RNA content was increased 8.6%, DNA content 10%; and DNA specific activity 24% in DMH-treated mice. RNA:DNA ratio in DMH-treated mice was the same as in controls. Mice receiving DMH and DFMO had no increase in crypt depth. Crypt depth in mice taking DFMO alone was also the same as controls. After 28 weeks treatment with DFMO there was a fall in putrescine (PUT) content (46-63%); a fall in spermidine (27-38%) and a rise in spermine (18-22%). PUT was 31.3% higher in DMH-treated mice than controls. At 28 weeks 13 out of 17 mice (76%) treated with DMH alone had histologically confirmed colon tumors. Two out of 18 (11%) mice treated with DMH and DFMO had colon tumors. Fifty colon carcinomas were present in 16 DMH-treated mice; a total of 3 colon tumors was present in 3 of the mice treated with DMH and DFMO. Inactivation of colonic ODC by continuous feeding of DFMO results in partial depletion of cellular polyamines and a greatly reduced incidence of DMH-induced colon carcinomas. (no Refs)

29. INFLUENCE OF ORAL SUPPLEMENTATION OF ASCORBATE UPON THE INDUCTION OF N-METHYL-N'-NITRO-N-NITROSOGUANIDINE.

Kawasaki H, Morishige F, Tanaka H, Kimoto E
(c/o Kimoto) Dept. Chemistry, Faculty Science, Fukuoka Univ., 11 Nanakuma, Nishi-ku, Fukuoka 814, Japan
Cancer Lett; 16(1):57-63 1982

The influence of oral supplementation of ascorbic acid (AA) upon the induction of N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) gastric cancer was investigated in young male Wistar rats. When MNNG-initiated rats (167 ug/ml in the drinking water) were fed a diet containing a daily dose of 0.4 g sodium ascorbate (AA), no significant tumor inhibition was observed, although AA supplementation reduced the grade of the lesion to some extent. When AA supplementation was not begun until 210 days after MNNG, at a time when adenomatous hyperplasia of the stomach epithelium was evident, again, no significant tumor inhibition was observed. AA supplementation in these animals did result in a significant reduction in the grade of the gastric lesions produced, however. Though adenocarcinoma cells seemed to be induced in AA supplemented animals, their downward massive growth, as occurred in animals not supplemented with AA, was inhibited by a heavy proliferation of connective tissue fibers surrounding them. Tumor masses were thus effectively encapsulated by connective tissue in AA supplemented animals. (14 Refs)

30. DNA-METHYLATION BY NITROSOCIMETIDINE AND N-METHYL-N'-NITRO-N-NITROSOGUANIDINE IN THE INTACT RAT.

Gombar CT, Magee PN
Fels Res. Inst., Temple Univ. Sch. Medicine, Philadelphia, PA, 19140
Chem Biol Interact; 40(2):149-157 1982

The ability of the nitroso derivative of the drug cimetidine to interact with cellular macromolecules in the intact rat was investigated. Radio-labeled nitrosocimetidine was shown to methylate DNA in a variety of tissues in the rat after oral administration. Radioactivity was also detected in the RNA and protein extracted from these same tissues. Methylation of DNA by the parent compound, cimetidine, as not detected in any of the tissues studied. For comparison, the DNA methylation produced by the carcinogen N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) dosed orally was measured. DNA alkylation by MNNG was found to be approx 2-36x greater than that produced by NC, varying with the tissues studied. The highest yield of DNA alkylation was found in the stomach for MNNG and the small intestine for nitrosocimetidine suggesting pharmacokinetic differences. (Author abstract) (23 Refs)

31. INTESTINAL ADAPTATION AND EXPERIMENTAL CARCINOGENESIS AFTER PARTIAL COLECTOMY. INCREASED TUMOUR YIELDS ARE CONFINED TO THE ANASTOMOSIS.

Williamson RC, Davies PW, Bristol JB, Wells M
Univ. Dept. Surgery, Bristol Royal Infirmary, Bristol BS2 8HW, England
Gut; 23(4):316-325 1982

Small-bowel resection enhances experimental colorectal carcinogenesis, probably by stimulating epithelial cell proliferation. The possibility that similar mechanisms might explain metachronous large-bowel cancers in man was tested in Sprague-Dawley rats submitted to partial colectomy before or after a 5-wk course of azoxymethane (total dose 50 mg/kg). The timing of operation did not affect tumor yields at 40 wk. Cecal resection augmented mucosal mass in the ileum and right colon but did not affect carcinogenesis. Right hemicolectomy only increased ileal segmental wt (by 22%); left hemicolectomy increased the protein and DNA contents of the residual right colon by 18-42%. Large-bowel tumors in 84 rats were distributed as follows: proximal colon 36, colonic anastomosis 51, distal colon 87, rectum 43. Consistent with this left-sided predominance, left hemicolectomy reduced the number of large-bowel tumors. A twofold increase in distal tumors after both transection and right hemicolectomy simply reflected the high incidence of anastomotic tumors. Furthermore, one rat given vehicle as opposed to carcinogen developed an invasive mucinous adenocarcinoma at the colorectal anastomosis, after left hemicolectomy. The large bowel shows limited adaptation to partial resection and is not at increased risk of carcinogenesis, except in the region of the suture line. (Author abstract) (48 Refs)

32. MECHANISM OF ESOPHAGEAL TUMOR INDUCTION IN RATS BY N-NITROSOMETHYLBENZYLAMINE AND ITS RING-METHYLATED ANALOG N-NITROSOMETHYL(4-METHYLBENZYL)AMINE.

Hodgson RM, Schweinsberg F, Wiessler M, Kleihues P
(c/o Kleihues), Pathologisches Institut, Albertstrasse 19, 78 Freiburg, W. Germany
Cancer Res; 42(7):2836-2840 1982

The metabolism of the esophageal carcinogen N-nitrosomethylamine (MBN) and its ring-methylated analog N-nitrosomethyl(4-methylbenzyl)amine (4-MeMBN) were investigated in male Wistar rats. When given in drinking water, both compounds have been shown to induce a high incidence of esophageal carcinomas but, after systemic administration of equimolar doses, 4-MeMBN is considerably less toxic and carcinogenic than in MBN. The data indicate that the lower toxicity and carcinogenicity of 4-MeMBN after systemic administration are due to the rapid formation (mainly in the liver) and excretion via the urine of its benzoic acid derivative. The strong carcinogenic effect of po 4-MeMBN can be explained by direct uptake from the drinking water into the esophageal mucosa. Following a single iv injection of [methylene-14C]MBN and 4-Me[methylene-14C]MBN, no benzylated bases were detectable in rat tissues. This indicates that the bioactivation of these compounds is initiated predominantly by hydroxylation at the methylene bridge leading to a methylating rather than a benzylating intermediate as the ultimate carcinogen. (14 Refs)

33. INFLUENCE OF DAILY SUBCUTANEOUS ADMINISTRATION OF 6-METHYLPREDNISOLONE AND ORAL APPLICATION OF 30% SALINE SOLUTION ON TUMORIGENESIS INDUCED IN MOUSE STOMACH BY SINGLE APPLICATION OF 7,12-DIMETHYLBENZ(A)ANTHRACENE.

Wagner G, Habs M, Schmahl D
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J Cancer Res Clin Oncol; 103(2):207-209 1982

Low-dose dimethylbenz(a)anthracene (25 mg/kg po by gavage on day 1) produced papillomas in the forestomach of female C57BL/6 mice treated with 6-methylprednisolone (MP: 80 mg/kg/day sc on days 1-3) and 30% NaCl (0.25 ml/animal, days 1-3, 1 hr after MP, by gavage). Hyperplasia/hyperkeratosis was observed in 5/20 animals and papilloma in 12/20 animals. Median latent period for papilloma development was 25 days. The results indicate that in an altered environment small amounts of a chemical carcinogen suffice to induce tumors. (7 Refs)

34. MUTAGENICITY AND SYNTHESIS OF ALPHA-SUBSTITUTED N-NITROSAMINES: DERIVATIVES WITH DITHIOCARBAMIC ACID.

Pool BL, Bertram B, Wiessler M
Inst. Toxicology and Chemotherapy, German Cancer Res. Center, Im Neuenheimer Feld 280, 6900 Heidelberg, W. Germany
Carcinogenesis; 3(5):563-567 1982

Disulfiram (DSF) can considerably alter the organotropy of chemical carcinogens. For N-nitrosodimethylamine and for N-nitrosodiethylamine the organotropy is shifted from the liver to the nasal cavity or the esophagus, respectively. Whereas the influence of DSF or its metabolites on enzyme systems has been studied, little is known about its interaction with the carcinogens at a molecular level. Therefore, postulated reaction products of a series of alpha-hydroxylated N-nitroso-dialkylamines and dithiocarbamate were synthesized and tested for mutagenicity in Salmonella typhimurium TA 1535. The results show that the compounds conjugated at a primary alpha-C-atom are not mutagenic, whereas those conjugated at a secondary alpha-C-atom are active. The primary N-nitroso-dithiocarbamates represent unique examples of inactivated dialkyl-nitrosamine derivatives. In addition, their formation in vitro was indirectly demonstrated. The possible role these inactivated compounds may play during the DSF-modulation of carcinogenesis will be discussed. (Author abstract) (16 Refs)

35. ESOPHAGEAL AND HEPATIC MICROSOMAL METABOLISM OF N-NITROSOMETHYLBENZYLAMINE AND N-NITROSODIMETHYLAMINE IN THE RAT.

Labuc GE, Archer MC
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Cancer Res; 42(8):3181-3186 1982

The metabolism of the rat esophageal carcinogen N-nitrosomethylbenzylamine (NMBzA) was studied using microsomes prepared from liver and esophageal mucosa of untreated male Sprague-Dawley rats. NMBzA was extensively metabolized to benzaldehyde, benzyl alcohol, and formaldehyde by hepatic microsomes. The rate of metabolism at the benzyl moiety was 10-fold higher than that at the methyl moiety. Mucosal microsomes metabolized NMBzA to benzaldehyde and formaldehyde at rates one-fifth and one-sixtieth of those in the liver, respectively; benzyl alcohol formation was undetectable. Esophageal metabolism of NMBzA was exclusively located in the mucosa, preferentially in the microsomal fraction, was reduced nicotinamide adenine dinucleotide phosphate dependent, and was inhibited CO and 2-diethylaminoethyl-2,2-diphenylvalerate. A low level of cytochrome P-450 was detected in the mucosal microsomes. Whereas hepatic metabolism of NMBzA was inducible by phenobarbitone pretreatment, mucosal metabolism was not altered by either phenobarbitone or 3-methylcholanthrene pretreatment. The hepatocarcinogen N-nitrosodimethylamine was extensively metabolized by hepatic microsomes to formaldehyde, but demethylation was not detected in the microsomes from esophageal mucosa, a nontarget tissue. The results indicate that rat esophageal mucosa contains an enzyme system which metabolized NMBzA at a high rate and exhibits properties typical of cytochrome P-450. This enzyme may play a role in determining which compounds induce tumors in rat esophagus. (Author abstract) (26 Refs)

BIOCHEMICAL, MORPHOLOGICAL AND IMMUNOLOGICAL ASPECTS OF GI CARCINOGENESIS

36. IDENTIFICATION OF CARCINOGENS BY MEASUREMENT OF CELL-MEDIATED IMMUNITY: II. ASSAY SPECIFICITY.

Stevens RH, Cole DA
Dept. Radiology, Radiation Res. Lab., Univ. Iowa, Iowa City, IA, 52242
Environ Res; 28(1):67-76 1982

Studies utilizing the Fischer F334 inbred rat model were undertaken to define the specificity for antitumor cell-mediated immune (CMI) measurements as determined by lymphoid-cell cytotoxicity to determine whether such values could serve as an analytical reflection for the carcinogenic potential of environmental pollutants. The investigations revealed that specificity was apparently limited to a carcinogenic insult and designated by the embryonic origin of the affected tissue. For example, it was found that animals having x-ray-induced small-bowel, 1,2-dimethylhydrazine-induced colon, and 7,12-dimethylbenz[a]anthracene-induced pancreas adenocarcinomas possessed lymphoid cells cytotoxic to tumor target cells of either the small bowel or pancreas, but were not lytic to tumor tissue of ectodermal or mesodermal origin. Nor was injury inflicted upon normal intestinal, kidney, or tail fibroblastic cells, while significant lysis was seen when normal fetal cells were used as targets. The findings also suggest that the presence of the carcinogen in the assay has little influence upon the CMI values. Thus, the present investigation continues to support the concept that immunological responsiveness may serve as a useful measure for specifically identifying and quantitating effects of environmental carcinogens. (Author abstract) (23 Refs)

37. ARGYROPHIL CELLS IN EARLY GASTRIC CARCINOMA: AN IMMUNOHISTOCHEMICAL AND ULTRASTRUCTURAL STUDY.

Tahara E, Ito H, Shimamoto F, Taniyama K, Iwamoto T, Sumiyoshi H, Kajihara H, Yamamoto M
First Dept. Pathology, Hiroshima Univ. Sch. Medicine, 1-2-3 Kasumi, Minami-ku, Hiroshima 734, Japan
J Cancer Res Clin Oncol; 103(2):187-202 1982

Eighteen argyrophil cell carcinomas in 101 early gastric carcinomas were examined histologically, ultrastructurally, and immunohistochemically for polypeptides, carcinoembryonic antigen (CEA), lysozyme, and human chorionic gonadotrophin (hCG). Seven of these 18 tumors had gastrin, and 2 of 7 tumors also contained somatostatin. In all of these 18 tumors CEA were demonstrated. Seven had lysozyme and 5 of 7 tumors also contained gastrin; hCG were present in 4 of 18 tumors and 2 of 4 tumors had gastrin, CEA, mucin, and lysozyme simultaneously. Argentaffin cells were found in 7 of 18 tumors. Of the above seven tumors containing gastrin, three had argentaffin cells. Ultrastructurally, several types of secretory granules were noted and tumor cells resembling D1-or P cells were present in 9 of the 18 tumors. Macroscopically, many of the tumors showed IIc or IIc + III type. Histologically, the 18 tumors consisted of 6 well differentiated adenocarcinomas and 12 poorly differentiated adenocarcinomas including signet-ring cell carcinoma. These 12 tumors frequently developed in the stomach of young females. In view of our previous investigation, it was suggested that the IIc-type argyrophil cell carcinoma histologically showing poorly differentiated adenocarcinoma may be related to scirrhous carcinoma of the stomach. (Author abstract) (30 Refs)

38. LIPID CLEARANCE IN A COLONIC TUMOUR MODEL IN RATS (MEETING ABSTRACT)

Windle R, Bell PR
Department of Surgery, University of Leicester, Royal Infirmary, Leicester, England
Twenty-third Annual General Meeting of the British Association for Cancer Research, March 29-31, 1982, Edinburgh, Scotland. British Association for Cancer Research 78 pp., 1982.

Marked derangement of fat metabolism occurs in cancer. Body fat is lost and serum triglyceride (TG) levels may be elevated. Although adipose tissue lipolysis is increased in experimental cancer an alternative explanation may be that there is a reduction in turnover of circulating TG. This may be measured by the clearance of an exogenous lipid emulsion load. In order to test this hypothesis lipid clearance has been measured with TG levels during the induction of a colorectal cancer model in rats. Tumors were induced by 15 weekly injections of 15 mg/kg dimethylhydrazine (DMH). Serum TG levels and the rate of clearance of intravenous lipid emulsion (0.5ml/kg of 20% intralipid) were measured before DMH and 8 weekly thereafter in 6 groups of 12 fasted rats. Groups of age matched rats not given DMH acted as controls. Tumors appeared at 30 weeks in the DMH groups. TG levels were reduced by 18% at 16 and 24 weeks and then became raised by 33% over pretreatment levels at 48 weeks, by which time the animals had lost 15-20% of their body weight. Lipid clearance was significantly increased at 16 and 24 weeks and then reduced by half at 48 weeks. Administration of heparin at 48 weeks increased lipid clearance and reduced TG levels. There was no change with time in TG levels or in lipid clearance rate in the control groups. In conclusion, TG levels are related to the rate of lipid turnover. The early depression of clearance may have been caused by DMH. A large tumor load was associated with raised TG levels and a reduction in turnover. (3 Refs)

39. DNA CONTENT AS A MARKER OF PRE-CANCEROUS LESIONS OF THE DIGESTIVE TRACT (MEETING ABSTRACT).

Capurso L, Teodori L, DeVita R, Galloni L, Tarquini M, Mauro F, Nervi C, Pallone F
Cattedra Gastroenterologia Universita, Rome, Italy
Gastroenterology; 82(5,part2):1029 1982

In order to detect the abnormality of the DNA content distribution as a marker of precancerous or early cancerous lesions of the digestive tract, human endoscopic biopsies have been analyzed. Samples were derived from stomach, duodenum and colon of normal donors and of patients clinically classified as affected by non-neoplastic lesions such as ulcer, atrophic gastritis, chronic gastritis and polyps. Sample processing has been performed by mechanical and enzymatic treatment (collagenase and haluronidase vs pepsin treatment revealed no significant changes in the DNA pattern). Staining for flow cytometric analysis (Phywe Ortho ICP 22) has been achieved by ethidium bromide and mithramycin. Normal samples exhibited the usual DNA distribution with G1/0,S and G2/M compartments. An aneuploid cell subpopulation was found in 4/7 atrophic or chronic gastritis specimens. Such aneuploidy is similar to that typical of gastric adenocarcinoma, DNA index ranging from 1.1 to 1.4 in comparison to 1.0. However, the percent aneuploid cells in the majority of tumors was generally higher than in aneuploid gastrites. Furthermore, polyps also exhibited an aneuploid peak, while ulcers were characterized by a normal, diploid DNA content. It is likely that the occurrence of aneuploidy in non-neoplastic lesions reflects some pre-cancerous situation or the presence of an early, small fraction of neoplastic cells. (no Refs)

40. GASTROINTESTINAL INVOLVEMENT IN KAPOSI'S SARCOMA (MEETING ABSTRACT).

Saltz RK, Kurtz RC, Lightdale CJ, Safai B, Myskowski P, Urmacher C
Department of Medicine and Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY
Gastroenterology; 82(5,part2):1168 1982

Since September, 1981, we have evaluated ten male homosexual patients with biopsy-proven skin lesions of Kaposi's sarcoma. Nine are white, one is black, and their ages range from 32-50 (mean 40). We report the findings of upper gastrointestinal (UGI) endoscopy (8/10) and colonoscopy (7/10) in these patients. The typical appearing blue-red, raised, nodular Kaposi's lesions were identified in the stomach (4) and duodenum (2) in 5 of 8 patients. Biopsies were not initially positive because they were too superficial. Colonoscopy revealed normal findings in 4 patients, non-specific left-sided inflammatory changes in 2, and 1 patient had typical lesions of Kaposi's sarcoma in the sigmoid colon which were confirmed histologically. Three other patients with Kaposi's sarcoma have been seen. Autopsy done in two revealed diffuse GI involvement including the esophagus, stomach, small and large intestine, liver, spleen, and pancreas. We correlated the degree of skin involvement with the presence and location of the GI tract involvement. Eighty percent of those patients with advanced cutaneous disease had GI lesions. All of the patients with oral mucosal lesions had GI lesions. In one patient, treated with Interferon, in whom improvement of cutaneous lesions was seen, the UGI lesions also showed significant improvement. Seven of ten patients had blood type O+ which is twice the expected distribution of this blood type. Viral and immunologic studies are underway to further characterize this problem and attempt to identify etiologic agents. (no Refs)

41. ADENOSINE 3,5'-CYCLIC MONOPHOSPHATE DEPENDENT AND INDEPENDENT PROTEIN KINASE ACTIVITIES IN 1,2-DIMETHYLHYDRAZINE INDUCED RAT COLON CANCER.

Singh D, Loven DP, Stevens RH
Dept. Anatomy, Radiation Res. Lab., University Iowa, Iowa City, IA, 52242
Chem Biol Interact; 40(2):169-175 1982

The adenosine 3',5'-cyclic monophosphate (cAMP)-dependent and cAMP-independent kinase activities were measured in the 1,2-dimethylhydrazine (DMH) induced rat colon cancer and in untreated colon. Previous studies had shown that intestinal tumors induced by chronic exposure to DMH contained two-fold less intracellular cAMP. The present findings indicate that reduction in cAMP-dependent protein kinase activities also occur in colon cancer cells. Similar hydrogen ion dependence (pH 6-7) and approximate association constants (Ka approx 0.1 uM) were observed for the enzymes existing in both normal and tumor tissues, while the cAMP-dependent tumor protein kinase was found to phosphorylate phosvitin and casein to a greater degree. These recent findings are consistent with the concept that the concentrations of cAMP and activities of its associated enzyme system are inversely related to the cell proliferation state. (Author abstract) (22 Refs)

42. IN VIVO MEASUREMENTS IN FAMILIAL POLYPOSIS: KINETICS AND LOCATION OF PROLIFERATING CELLS IN COLONIC ADENOMAS (MEETING ABSTRACT).

Lightdale CJ, Lipkin M, Deschner E
Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Gastroenterology; 82(5,part2):1117 1982

In vivo measurements of the proliferation kinetics of epithelial cells in human adenomas were made following intravenous pulse injection of tritiated thymidine (3HTdR) in a patient with familial polyposis and Gardner syndrome. In the adenomas and in adjacent flat mucosa, biopsies were taken and microautoradiographs prepared at intervals after injection. Rates of epithelial cell proliferation, locations of proliferating cells within the crypts of adenomas and adjacent flat mucosa, fractions of 3HTdR-labeled mitoses and cells, and grain densities were analyzed. Results demonstrated the following: (1) A complete temporal cycle of proliferation of epithelial cells both in adenomas and in flat colonic mucosa, with cells completing only a single cycle during 4 days of observation; durations of G2 and S phases of the cell cycle were approximately 5 and 15 hours respectively both in adenomas and in flat mucosa; (2) After pulse injection, the locations of 3HTdR labeled epithelial cells within the adenomatous crypts revealed maximum proliferation near the lumenal surface; proliferation of labeled epithelial cells in flat mucosa occurred in the lower portion of the colonic crypts; (3) The locations of 3HTdR labeled epithelial cells at intervals after injection revealed mean migration rates of 0.4 cell positions per hour in the crypts of adenomas, and 0.3 cell positions per hour in crypts of adjacent flat mucosa; however, in contrast to the migration of epithelial cells toward the lumenal surface of the crypts in flat mucosa, in adenomas a markedly abnormal retrograde migration away from the surface of the mucosa occurred. (no Refs)

43. A NEW HUMAN COLON TUMOR CELL LINE, LS123 (MEETING ABSTRACT).

Rutzky LP, Siciliano MS, Giovanella BC, Noguchi PD, Kahan BD
The University of Texas Medical School and System Cancer Center, Houston, TX
In Vitro; 18(3,part2):294 1982

An epithelial cell line, LS123, was established in 1974 from the second of a series of three primary colon tumors resected from a Caucasian female. The tumor was a Dukes' B adenocarcinoma. Allozyme phenotyes of polymorphic enzyme loci had a frequency of 4x10(-3) and confirmed the independent genetic origin of this line. Although the line is heteroploid, it failed to display some properties associated with malignancy. Progressive tumors did not develop following inoculation of either 1 or 2x10(7) cells into N:NIH(S)II or nu/nu Swiss nude mice, respectively. Colonies developed in the Hamburger-Salmon stem cell assay system, but not in 0.3% Bacto, Noble or agarose agars. LS123 cells formed colonies on confluent cell monolayers and were capable of serial growth in serum-free medium. Low concentrations of the tumor marker carcino-embryonic antigen (CEA) of 14.5x10(-5) ng CEA/cell were detected after 21 days of incubation. LS123 cells were invasive in the Chick Embryonic Skin assay system. Nests of glandular structures were observed in the skin, but little mitotic activity was present. The cells were well differentiated and resembled an abnormal colonic epithelium. (no Refs)

44. GASTRIC CARCINOMA WITH ARGYROPHILIC CELLS: LIGHT MICROSCOPIC, ELECTRON MICROSCOPIC, AND IMMUNOCHEMICAL STUDY.

Prade M, Bara J, Gadenne C, Bognel C, Charpentier P, Ravazzola M, Caillou B
Histopathologie-B, Institut Gustave-Roussy, rue Camille Desmoulins, 94800 Villejuif, France
Hum Pathol; 13(6):588-592 1982

An immunochemical study of a gastric adenocarcinoma with argyrophilic cells showed two areas of tumor that react differently with the usual histochemical reagents as well as with immune sera against gastrin and mucoprotein associated with antigens. Ninety percent of the tumor cells were PAS positive and contained M2 antigen, and some also contained M1 antigen. About 30% of the M2-positive cells stained strongly with an antigastrin serum as well as with the argyrophilic reagents. The remaining 10% of tumor cells were signet-ring cells located in several clumps in the tumor. These cells were positive for both PAS and alcian blue and contained intestinal M3 antigen. Forty-five percent of them also contained M1 gastric antigens. Carcinoembryonic antigen (CEA) was found in the cytoplasm of each tumor cell. The presence of CEA and M1 antigen together indicates a fetal pattern, suggesting that the cells originate from very immature gastrointestinal stem cells. (Author abstract) (16 Refs)

45. GASTRIC POLYPS; THEIR MORPHOLOGICAL AND ENDOSCOPICAL CHARACTERISTICS AND RELATION TO GASTRIC CARCINOMA.

Laxen F, Sipponen P, Ihamaki T, Hakkiluoto A, Dortscheva Z
Div. Gastroenterology, Second Dept. Medicine, Univ. Helsinki, 00290 Helsinki 29, Finland
Acta Pathol Microbiol Scand [A]; 90(3):221-228 1982

In 13,200 consecutive gastroscopies polyp-like lesions were found in 454 patients and of these 425 were examined histologically. Tumors other than polyps were excluded and there remained 357 cases which were divided in four groups: adenoma (8%), hyperplastic polyp (34%), foveolar hyperplasia (21%) and inflammatory polyp (36%). Transitional forms between different groups were seen and sometimes characteristics of different polyp types could be seen within one and same polyp. In addition, the mean age of the patients increased in order: inflammatory polyp, foveolar hyperplasia, hyperplastic polyp and adenoma, suggesting that the different groups are not separate entities but represent related stages in the morphogenesis of gastric polyps. Two hundred nineteen cases out of 357 patients were reexamined endoscopically on av 2.5 yr after the first examination. This examination revealed new polyps in 26% of all cases and spontaneous disappearance of the polyps in 14% of cases suggesting that gastric polyps, particularly those of the hyperplastic and inflammatory type are in a dynamically labile state. Gastric carcinoma was found in 27 (8%) of patients with polyps. In four of these cases the carcinoma was found at the reexamination (which in 3 cases was performed within 0.5 and 1 case within 1.5 yr). In 14 cases carcinoma was found inside the polyps and in 6 of these carcinoma was 'early' in its growth. In 13 cases carcinoma was found outside the polyps and in all of these carcinoma was 'advanced'. Carcinoma was found in 38% of adenoma cases and in 5% of cases with polyps other than adenomas. (Author abstract) (26 Refs)

46. IDENTIFICATION OF TWO DIVIDING CELL POPULATIONS IN THE RAT JEJUNUM WHICH RESPOND DIFFERENTLY TO X-RAYS (MEETING ABSTRACT)

Barnes PG, Wright NA
Department of Histopathology, Royal Postgraduate Medical School, Du Cane Road, London W12 OHS, England
Twenty-third Annual General Meeting of the British Association for Cancer Research, March 29-31, 1982, Edinburgh, Scotland. British Association for Cancer Research 78 pp., 1982.

A method has been devised for the investigation of any heterogeneity of cellular response to cytotoxic agents that may arise with respect to differentiation and with respect to position in the cell cycle. From studies over a time course following exposure to a wide range of doses of x-rays, it has been found that: 1) The populations of cells in the last transit cell cycle (a) undergoes death via liquefaction necrosis, (b) is the population from which survivors give rise to clonal repopulation after exposure to high doses. 2) The population of cells in previous transit cell cycles (a) produces a large number of autophagosomes that contain nuclear material within 2 hr of irradiation, (b) is unusually sensitive to a rapid, interphase cell death. The biological origin of these differences is a matter of speculation. Identification of the point at which the differentiating progeny of the function stem cells are no longer potential stem cells has previously been a matter of conjecture. These studies provide definitive evidence that cells lose their 'stemness' at the last transit division. Two implications of this result are that this cell renewal system (a) functional organization appears to differ from that in the hemopoietic system where multipotential 'stemness' is lost promptly upon differentiation, (b) that arguably all dividing epithelial cells in tumors of the intestine may be clonogeneic, as in normal tissue. (no Refs)

47. THE EFFECT OF DERIVATIVES OF FOLIC ACID ON THE FLUORODEOXYURIDYLATE-THYMIDYLATE SYNTHETASE COVALENT COMPLEX IN HUMAN COLON XENOGRAFTS.

Houghton JA, Schmidt C, Houghton PJ
Dept. Biochemical and Clinical Pharmacology, St. Jude Children's Res. Hosp., 332 North Lauderdale, Memphis, TN, 38101
Eur J Cancer Clin Oncol; 18(4):347-354 1982

This study was designed to examine the endogenous concentrations of 5,10-methylenetetrahydrofolate (CH2FH4) in human colorectal adenocarcinoma xenografts, and to determine the ability of other folate derivatives to increase the formation of the ternary covalent complex between CH2FH4, [6-3H]-5-fluorodeoxyuridylate (FdUMP) and thymidylate synthetase (TS, EC 2.1.1.45). Levels of CH2FH4 were determined by measuring the release of [3H]2O from [5-3H]-dUMP using TS from Lactobacillus casei. The reaction was linear from 1.9 x 10(-13) to 2.4 x 10(-11) mol of CH2FH4 assayed. Concentrations of CH2FH4 were low, ranging from 66 to 233 nM in cell water. Tetrahydrofolate (FH4) and dihydrofolate (FH2) and 5-methyltetrahydrofolate (5-CH3FH4) decreased the covalent binding of [6-3H]-FdUMP in vitro. Administration of FH4 or FH2 to tumor-bearing mice reduced subsequent formation of the covalent complex in vitro. Since 5-CH3FH4 is a major derivative of folate in mammalian tissues, its effect on the covalent binding of [6-3H]-FdUMP was examined further; even in the presence of homocysteine and cyanocobalamin (B12), the formation of the covalent complex was not increased. The fate of [5-14CH3]-FH4 was subsequently examined in vivo. In tumors at 1 hr after injection, 72% of the radiolabel remained as [5-14CH3]-FH4, while 17% had been converted to [14C]-methionine or incorporated into protein. By contrast, however, the incorporation of radiolabel into the protein fraction of liver was almost 30-fold greater at this time. At 4 hr, radioactivity in tumors (dpm/g) and in the fraction associated with [5-14CH3]-FH4 was decreased by over 60%, while metabolism was increased by only 13%. No polyglutamate forms of [5-14CH3]-FH4 were detected in tumors at 4 hr after treatment. (Author abstract) (38 Refs)

48. UPTAKE OF [3H]THREONINE IN HUMAN COLONIC MUCOSA ASSOCIATED WITH CARCINOMA: AN AUTORADIOGRAPHIC ANALYSIS AT THE ULTRASTRUCTURAL LEVEL.

Dawson PA, Filipe MI
Dept. Histopathology, Westminster Medical Sch., Udall St., London SW1P 2PP, England
Histochem J; 14(3):385-401 1982

[3H]Threonine uptake was studied by electron microscopical autoradiography using the method of statistical analysis of Blackett and Parry. The results are discussed in the light of [3H]galactose studies. The changes in protein uptake are compared with different isotope incubation periods and with pulse-labeling techniques. Mean reactive values, including the standard errors, for the control and the 'transitional' mucosa with [3H]threonine labeling for the various organelles are presented. Results indicated that the increased uptake of [3H]threonine in transitional mucosa appears to be the result of prolonged protein synthesis associated with an extension of the cellular proliferation zone in the crypt rather than being an effect of increased cell turnover. (14 Refs)

49. CHANGES IN [3H]GALACTOSE UPTAKE IN HUMAN COLONIC MUCOSA WITH CARCINOMA: AN ULTRASTRUCTURAL STUDY.

Lawson PA, Filipe MI
Dept. Histopathology, Westminster Medical Sch., Udall St., London SW1P 2PP, England
Histochem J; 14(3):361-383 1982

Uptake of [3H]galactose was studied by electron microscopical autoradiography both on the basis of isotope uptake over a period of time and with pulse labeling to investigate the changes in the glycoprotein synthesis associated with malignancy in the colonic mucosa. Normal mucosa and mucosa adjacent to tumor ('transitional') from human large bowel specimens resected for carcinoma were compared. The most marked differences were found in the middle and upper crypt; the region of differentiation being the middle crypt in all types of tissue and the upper crypt being a region of extended immaturity in transitional mucosa. (24 Refs)

50. HUMAN CELL LINE OF PANCREATIC ADENOCARCINOMA (MEETING ABSTRACT).

Morgan RT, Moore GE, Semple TU, Gordon SG, Lewis B
Denver General Hospital and University of Colorado Health Science Center, Denver, CO, 80262
In Vitro; 18(3,part2):294 1982

A continuous cell line LVP-BL was established from a liver metastasis in a 36-year old white male with pancreatic adenocarcinoma. LVP-BL grew in small tight colonies of pleomorphic epithelioid cells adherent to the culture vessel in RMPI 1640 medium or GEM 1717 medium supplemented with 5% to 20% heat-inactivated fetal bovine serum and antibiotics. LVP-BL was tested for growth in GEM 1717 medium supplemented with 10% Hespan (Hetastarch 1.2% v/v) and cellular viability and typical cellular morphology were maintained for up to 14 days. LVP-BL secreted elastase (2.09 ng/ml), trypsin (0.36 ug/ml) but no chymotrypsin. No carcinoembryonic antigen or adrenocorticotropic hormone production were detected. LVP-BL possessed no receptor proteins for estrogen, progesterone, androgen, or dexamethasone. Five allozymes were assayed. Ultramorphology studies revealed immature reticulated nucleoli with randomly scattered chromatin in the nuclei. Cytoplasm contained few tonofibrils, extensive rough endoplasmic reticulum, numerous glycogen vacuoles, abnormal mitochondrial and sparse desmosomes. Individual cells had sparse random microvilli. Cytogenetic analyses showed chromosome number per metaphase ranged from 47 to 90. Marker chromosomes were identified. (no Refs)

51. PRESENCE OF AN UNUSUAL ALKALINE PHOSPHATASE IN CULTURED HUMAN RECTAL CANCER CELLS (MEETING ABSTRACT).

Morita A, Kim YS
Department of Medicine, Veterans Administration Medical Center and University of California, San Francisco, CA, 94121
Gastroenterology; 82(5,part2):1134 1982

Alkaline phosphatase (AP) has been shown to be localized on cellular membranes and in humans it has been proposed that there are at least three structural genes which determine different forms of AP. These isozymes can be easily distinguished by a number of biochemical parameters. However, we have found an unusual AP which does not fall into any of the three isozyme classes in a human rectal cancer cell line, HRT-18. The cells were cultured in mono-layer. Cytosol and total membrane fractions were isolated by centrifuging the cell homogenate at 100,000 x g for one hour. AP activity was assayed in bicarbonate (BC) or 2-amino-2-methyl-1-propandiol (AMPD) buffer, pH 10.0 using p-nitrophenyl phosphate as substrate. The enzyme in the cell homogenate was found to be heat-stable and inhibited by phenylalanine, but not by homoarginine with BC buffer. When AMPD buffer was used, the enzyme was heat-labile and resistant to both phenylalanine and homoarginine. In AMPD buffer enzyme activity was two times higher as compared to BC buffer. The enzyme required Mg++ when assayed in AMPD buffer, while the addition of Mg++ showed minimum effect when BC buffer was used. When the subcellular distribution of AP was examined, over 80% of the enzyme activity was associated with the membrane fraction in the case of BC buffer, whereas about 65% of the activity was found in the cytosol with AMPD buffer. Regardless of the buffers employed the membrane bound enzyme was heat-stable and inhibited by phenylalanine but not by homoarginine. (no Refs)

PANCREATIC CARCINOGENESIS

52. EXPERIMENTAL PANCREATIC CARCINOGENESIS.

Longnecker DS
Dept. Pathology, Dartmouth Medical Sch., Hanover, NH
Lab Invest; 46(5):54[illegible]-544 1982

Classification of experimental pancreatic neoplasms is discussed. The spectra of histologic types of experimentally induced pancreatic neoplasms which arise from acinar and ductal epithelium appear to overlap. Early biochemical and immunologic markers may be different for neoplasms of acinar cell and ductal cell origin; such a difference could influence approaches to early diagnosis. Factors affecting promotion and inhibition of the two types of pancreatic tumors may also be different. (6 Refs)

53. TWO POPULATIONS OF CELLS WITH DIFFERING PROLIFERATIVE CAPACITIES IN ATYPICAL ACINAR CELL FOCI INDUCED BY 4-HYDROXYAMINOQUINOLINE-1-OXIDE IN THE RAT PANCREAS.

Rao MS, Upton MP, Subbarao V, Scarpelli DG
Dept. Pathology, Northwestern Univ. Medical Sch., 303 East Chicago Ave., Chicago, IL, 60611
Lab Invest; 46(5):527-534 1982

A single intravenous injection of 4-hydroxyaminoquinoline-1-oxide in male Wistar rats at a dose of 6 mg per kg of body weight induced atypical acinar cell foci in 100% of the animals. Atypical acinar cell foci could be classified histologically as basophilic and acidophilic foci and acidophilic nodules. Cells in basophilic foci were large, contained an irregular nucleus and a markedly basophilic cytoplasm with a few to small number of zymogen granules (zymogen-poor cells). By transmission electron microscopy, these cells showed markedly irregular plasma membranes, a well-developed rough endoplasmic reticulum and a few zymogen granules. Cells in acidophilic foci and nodules contained an intensely eosinophilic granular cytoplasm (zymogen-rich cells) and a large oval to round nucleus. By transmission electron microscopy, the cells showed zymogen-rich cytoplasm and irregular lateral plasma membranes. Mitotic activity was completely absent or very rarely observed in normal pancreas or basophilic foci, in contrast to acidophilic foci and nodules in which a mean value of 2.75 +-1.27 per 1,000 cells was found. Autoradiography confirmed these differences between the proliferative capacity of cells in basophilic foci (1 +-1 labeled nuclei per 1,000 cells) and acidophilic foci (23.2 +-3.15 labeled nuclei per 1,000 cells). These studies indicate that 4-hydroxyaminoquinoline-1-oxide induces two types of atypical acinar cell foci with different morphologic features and proliferative capacity. (Author abstract) (35 Refs)

54. HISTOCHEMICAL ELUCIDATION OF HAMSTER PANCREATIC CARCINOGENESIS INDUCED BY N-NITROSO-BIS(2-HYDROXYPROPYL) AMINE.

Miyazaki K, Takasan H, Hamashima Y
1st Dept. Surgery, Faculty Medicine, Kyoto Univ., Sakyo-ku, Kyoto 606, Japan
Nippon Geka Hokan; 51(1):3-13 1982

Hamster pancreatic carcinogenesis induced by 500 mg/kg/wk sc N-nitroso-bis(hydroxypropyl) amine (DHPN) was studied in 20 outbred 8-wk-old Syrian golden hamsters. Pathological and histological changes were observed 4-27 wk after the induction of carcinogenesis. The most frequent change observed was multilayer hyperplasia of intralobular ductules. After 22 wk adenocarcinomas were observed. The distribution and intensity of enzyme activity is listed. In adenocarcinomas, strong activities of alkaline phosphatase, succinate dehydrogenase, lactate dehydrogenase (LDH), glucose-6-phosphatase (G-6-PD), and NADH-tetrazolium reductase were observed. Moderate activity of LDH and G-6-PD was proved in the epithelium of adenocarcinomas. In the control group, 3H-thymidine uptake (TU) was observed in all tissues components. TU of the acinar cells, interlobular ductules (ILD), and main pancreatic ducts was greater than that of islet cells. After DHPN administration, a significant increase of TU was observed. No TU increase was observed in islet cells. TU of flat epithelial and hypertrophic multiplications and multilayer hyperplasia of ILD was greater than in controls. TU of hypertrophic epithelial multiplications was significantly greater than that of flat. TU of adenocarcinoma epithelium was significantly greater than that of other lesion and normal tissue components. The differences of serum ribonuclease and amylase activity between DHPN-treated and control animals are presented. (17 Refs)

55. ESTABLISHMENT AND CHARACTERIZATION OF TWO HUMAN PANCREATIC CANCER CELL LINES TUMORIGENIC IN ATHYMIC MICE.

Dexter DL, Matook GM, Meitner PA, Bogaars HA, Jolly GA, Turner MD, Calabresi P
Dept. Medicine, Roger Williams General Hosp., 325 Chalkstone Ave., Providence, RI, 02908
Cancer Res; 42(7):2705-2714 1982

Two human pancreatic cancer lines, RWP-1 and RWP-2, have been established from two patients with primary pancreatic cancer metastatic to the liver. The patients' tumors, the xenografted tumors, and tumors obtained by inoculation of nude mice with cultured RWP-1 and RWP-2 cells are all moderately-well-differentiated ductal cell adenocarcinomas. Ultrastructural analysis supports the tissue histopathology findings. Xenografts of RWP-1 tumors double every 10 days, whereas the doubling time of RWP-2 xenografts is 22 days. Both tumors contain mucin. RWP-1 and RWP-2 cells have a doubling time in culture of 45 hr and form colonies in soft agar. RWP-1 cultures appear to be morphologically heterogenous; two distinct epithelial cell types can be identified. RWP-1 and RWP-2 have modal chromosome numbers of 64 and 62, respectively. Appreciable levels of glucose-6-phosphate dehydrogenase and lactic dehydrogenase were found in both cell lines and xenografts. RWP-1 and RWP-2 cells produce appreciable amounts of carcinoembryonic antigen, 1,090 and 414 ng/10(6) cells, respectively. (Author abstract) (51 Refs)

56. BINDING OF [14C]-AZASERINE TO DNA AND PROTEIN IN THE RAT AND HAMSTER.

Zurlo J, Coon CI, Longnecker DS, Curphey TJ
New York Univ. Medical Center, Inst. Environmental Medicine, 550 First Ave., New York, NY, 10016
Cancer Lett; 16(1):65-70 1982

Binding and subsequent removal of radioactivity in DNA and protein of various target and nontarget organs after administration of 14C-azaserine were compared in Lewis rats and Syrian golden hamsters. Rats develop acinar cell abnormalities and pancreatic tumors in response to AS treatment, while hamsters do not. In rats, after 90 min the greatest amount of binding to DNA occurred in the liver, while binding to DNA of pancreas and kidney occurred to a leser extent. After 24 hr, 55% of the DNA-associated radioactivity had been removed from liver, 16% from kidney and 49% from pancreas, bringing the specific activity of DNA in these three organs to nearly the same level. Protein from liver also exhibited higher specific activity than did that from the other organs 90 min after AS treatment. While the levels of radioactivity in kidney and thymus were comparable in rat and hamsters, the specific activities of DNA and protein from hamster pancreas were each about 2x those from rat pancreas. Hamster liver DNA was also more extensively labeled than both rat liver DNA and hamster pancreatic DNA. These results indicate that binding of 14C-AS to DNA and protein do not correlate with species or tissue susceptibility to carcinogenesis by AS. (15 Refs)

57. EPIDEMIOLOGY OF HEPATIC, GALL BLADDER, AND PANCREATIC CANCER IN JAPANESE.

Aoki K, Sasaki R
Dept. Preventive Medicine, Nagoya Univ. Sch. Medicine, Nagoya, Japan
Nippon Rinsho; 40(1):8-14 1982

Factors affecting the occurrence of hepatic, gall bladder, and pancreatic cancer were studied epidemiologically using death statistics. Of the three types of cancer, the age-adjusted death rate for both men and women between 1950-1978 was highest for hepatic cancer. The death rate for hepatic cancer between 1960-1975, was fairly steady for men, and was decreasing for women. There was a slight creeping up of rate between 1975-1978 in both men and women. The rates of death due to pancreatic or choledochal cancer showed an increase in both groups. According to birth cohorts, little change in death rates due to cancer were observed in the men born between 1890-1930. The death rates have decreased for the birth cohorts of women born since 1900. Deaths due to choledochal cancer increased for both men and women between 1969-1978. Higher rates of hepatic cancer were observed in both men and women living in Kyushu and Yamagata Prefecture, in men living in Hiroshima and Osaka, and in women living in Tokushima. Death rates due to pancreatic cancer were high in Hokkaido

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and Aomori Prefecture. Although none of the three organs has direct contact with the outside environment, there is an increase in environmental carcinogenic factors. It was of interest that latent or complicated infections were observed frequently associated with the cancers. (43 Refs) (In JPN)

58. CANCER MORTALITY EXCESS.

Neuberger JS, Hollowell JG

Dept. Community Health, Univ. Kansas Sch. Medicine, Kansas City, KS

J Kans Med Soc; 83(5):244-248 1982

Cancer mortality by site and county in Kansas for the period 1973-1977 is reported. Data were restricted to white male and female residents of Kansas. Counties with elevated rates for 1950-1969 were compared with results for 1973-1977 to see if they remained consistently high for the same type of cancers. The only consistently high statistically significant mortality rates found in Kansas during both time periods were for lung cancer in white males in Cherokee and Wyandotte counties. Lung cancer mortality rates rose more rapidly than expected in females in Cherokee County to the point where lung cancer is presently comparable to breast cancer as the leading cause of female cancer mortality. Cancer sites which have increased in 1973-1977 to become statistically significantly elevated are male kidney cancer in Butler county, male bladder cancer in Shawnee county, and pancreatic cancer in Atchison county, (previously were not included). No significant excesses were found for females. Instability in rates due to small sample size were recognized as possible reasons for some of the calculated cancer mortality excess observed. (7 Refs)

59. SIGNIFICANCE OF THE SITE OF ORIGIN OF PANCREATIC EXOCRINE ADENOCARCINOMA.

Allen-Mersh TG

Whipps Cross Hosp., London E11, England

J Clin Pathol; 35(5):544-546 1982

The pancreatic head and neck constitute less than half (mean 46 +-5%) of the whole pancreas. There is no difference in the concentration of ductal epithelium between the head and the body of the pancreas. The preponderance of pancreatic exocrine tumors which arise in the head of the pancreas compared to the body is not, therefore, due to a larger number of cells at risk in the pancreatic head. This suggests that there is a greater risk of exocrine adenocarcinoma developing from the cells within the head of the pancreas than in those within the body of the pancreas. (Author abstract) (16 Refs)

60. PANCREATIC CANCER.

Cohn I

Dept. Surgery, Louisiana State Univ. Medical Sch., New Orleans, LA

Nippon Gan Chiryo Gakkai Shi; 17(2):241-249 1982

The incidence, etiology, prognosis, and types of cancer in the pancreas are discussed. One autopsy series showed that only 63/419 cases were primary to the pancreas. Among the 273 metastatic cases, the largest numbers arose in the breast, lung, stomach and colon or from melanoma. Some of the newer diagnostic procedures are discussed, as are operative procedures, use of radiotherapy, and some problems of diagnosis. (4 Refs)

REVIEWS AND OTHER RELATED STUDIES

61. CARCINOGENESIS AND BIOLOGICAL EFFECTS OF TUMOR PROMOTERS.

Hecker E

Inst. Biochemistry, German Cancer Res. Center, Heiodelberg, W. Germany

Carcinogenesis 7: 664 pp., 1982.

The most recent experimental findings on the etiological, cell biological, and molecular facets of carcinogenesis are reviewed. The basic problems of whether specific carcinogens function as promoters of carcinogenesis, as stimulators of initiation, or both, are addressed with respect to in vivo animal studies, epidemiological studies, and in vitro studies of tumor promotion. Carcinogenesis and tumor promotion in vivo is discussed with respect to the skin as a target tissue and nonepidermal target tissues. Effects of tumor promoters on cell proliferation and differentiation are reviewed for the epidermis and nonepidermal cell systems. Membrane interactions and receptors, effects on intercellular communication and cell metabolism, and viral and immunologic aspects are reviewed. Epidemiologic studies of esophageal cancer in Linxian County, China, nutritional carcinogenesis, and breast cancer as an example of promoting effects are discussed. (1368 Refs)

62. ESOPHAGEAL LEIOMYOSARCOMA.

Franklin GO, Antler AS, Thelmo WL, Rosenthal WS

Dept. Medicine, Westchester County Medical Center, Valhalla, NY, 10595

NY State J Med; 82(7):1100-1103 1982

A total of 57 well-documented cases of esophageal leiomyosarcoma now appear in the world literature. Analysis of these cases reveals that this rare tumor; although associated with squamous carcinoma in 10% of cases, behaves quite differently than squamous carcinoma in that it tends to be polypoid, rarely invasive, rarely metastatic, and may carry a far better prognosis when treated with surgical resection. More emphasis in the future, however, must be placed on determining whether or not similar risk factors exist as for squamous carcinoma and on studying longer-term survival patterns to learn more about the behavior of this interesting tumor. (Author abstract) (44 Refs)

63. ORGAN CULTURES FOR THE STUDY OF CHEMICAL CARCINOGENICITY (MEETING ABSTRACT).

Reiss B, Williams GM

American Health Foundation, Naylor Dana Institute for Disease Prevention, Valhalla, NY, 10595

In Vitro; 18(3,part2):289 1982

An in vitro system using organized tissue provides several advantages over in vivo and cell culture systems for the study of carcinogenesis; intercellular and intracellular processes as well as tissue interaction can be investigated in the precisely controlled environment of an organ culture system. Currently, several variations of basic organ culture methodologies for adult mammalian organs (colon, esophagus, trachea, skin, mammary gland, lung etc) produce long-term preservation of the epithelium with minimal histological or functional deviations from the normal in vitro condition. Several aspects of chemical carcinogenesis are under study in organ culture systems. The metabolism of carcinogens is being investigated directly, by examining the formation of metabolites in organ culture and, indirectly, by observing the acute molecular effects produced by reactive metabolites on the cultured tissue. Using these two parameters the metabolism of organ selective carcinogens has been documented in cultures of colon and esophagus. (no Refs)

64. THE DIFFUSE ENDOCRINE SYSTEM AND CARCINOIDS OF THE GASTROINTESTINAL TRACT: PART 1: ORTHOLOGICAL VIEWPOINTS AND GENERAL PATHOLOGY OF CARCINOIDS.

Borchard F

Pathologische Institut, Universitat Dusseldorf, Moorenstr. 5, D-4000 Dusseldorf, W. Germany

Z Gastroenterol; 20(4):187-205 1982

Carcinoids are epithelial tumors of the gastrointestinal tract that have potential endocrine activity and may become malignant. Eighteen distinct cell types have been identified, varying in histological structure, reactivity to silver salts, and the number and type of endocrine products. Small-cell anaplastic carcinomas contain endocrine granules and are highly malignant. Normal cells and carcinoids may exhibit a mixture of endocrine and exocrine differentiation. (87 Refs) (In GER)

65. BIOCHEMICAL MARKERS.

Higashino K, Sumikawa K

Third Dept. Internal Medicine, Osaka Univ. Sch. Medicine, Osaka, Japan

Nippon Rinsho; 40(1):43-50 1982

Biochemical markers used in diagnosing hepatic, bile duct, pancreatic, and other types of cancer are discussed. The common markers used in detecting cancer include C-reactive protein, glutamic oxaloacetic transaminase, glutamic pyruvic transaminase, lactate dehydrogenase (LDH), LDH4, LDH5, cholesterol, and serum amylase. Markers used to detect liver cancer include alpha-fetoprotein, alkaline phosphatase isoenzyme, gamma-guanosine triphosphate isoenzyme, ferritin, aldolase isoenzyme, 5'-nucleotidylphosphorodiesterase isoenzyme, and other newly discovered chemicals. Markers used to detect cancer of the bile duct or to distinguish cancerous from benign tumors include fetoprotein and alpha-antitrypsin. Markers for pancreatic cancer include pancreatic oncofetal antigen, carcino-embryonic antigen, ribonuclease, galactosyltransferase isoenzyme, and other chemicals. (44 Refs) (In JPN)

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CHEMICAL CARCINOGENESIS

1. TOXICITY OF POLYBROMINATED BIPHENYLS (PBBS) IN DOMESTIC AND LABORATORY ANIMALS.

Damstra T, Jurgelski W, Posner HS, Vouk VB, Bernheim NJ, Guthrie J, Luster M, Falk HL
Natl. Inst. Environmental Health Sciences, Post Office Box 12233, Research Triangle Park, NC, 22709
Environ Health Perspect; 44():175-188 1982

2. CHLOROFORM: A REVIEW OF ITS METABOLISM, TERATOGENIC, MUTAGENIC, AND CARCINOGENIC POTENTIAL.

Davidson IW, Sumner DD, Parker JC
(c/o Parker) ECAO, Environmental Protection Agency, MD-52, Research Triangle Park, MD, 27711
Drug Chem Toxicol; 5(1):1-87 1982

3. FORMALDEHYDE IN PRESENT-DAY ENVIRONMENTAL TOXICOLOGY.

Beritic T, Kovac S, Dimov D
Odjel za profesionalne bolesti, Institut za medicinska istrazivanja i medicinu rada, Zagreb, Yugoslavia
Arh Hig Rada Toksikol; 32(4):363-395 1981
In SCR

4. HORMONES AS ETIOLOGICAL AGENTS IN NEOPLASIA.

Furth J
Inst. Cancer Res., Columbia Univ. Coll. Physicians and Surgeons, New York, NY
Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.

5. CURRENT VIEWS ON HORMONES AND BREAST CANCER.

Molinatti GM, Limone P
Cattedra di Endocrinologia, Universita di Torino, C.so Polonia, 14, 10126 Turin, Italy
Minerva Med; 73(17):1047-1053 1982
In ITA

6. THE CHROMOSOMAL EFFECTS OF THE ORAL CONTRACEPTIVE.

Bishun NP
Tissue Culture and Cytogenetics Unit, Res. Dept., Marie Curie Memorial Foundation, The Chart, Oxted, Surrey, England
J Surg Oncol; 20(2):115-118 1982

7. TOXICITY AND CARCINOGENICITY OF NICKEL AND ITS COMPOUNDS. A REVIEW OF THE CURRENT STATUS.

Raithel HJ, Schaller KH
Institut fur Arbeits- und Sozialmedizin, Poliklinik fur Berufskrankheiten, Universitat Erlangen-Nurnberg, Schillerstrasse 25-29, D-8520 Erlangen, W. Germany
Zentralbl Bakteriol Mikrobiol Hyg [B]; 173(1/2):63-91 1981
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8. HISTORICAL OVERVIEW OF NITROSOUREA DEVELOPMENT.

Goldin A
Div. Cancer Treatment, NCI NIH, Building 37, Room 5E20, Bethesda, MD, 20205
INSERM Symp; 19:3-11 1981

9. PATHOLOGY.

Goyer RA
Natl. Inst. Environmental Health Sciences, Research Triangle Park, NC
JAMA; 247(21):2973-2975 1982

RADIATION CARCINOGENESIS

10. IDENTIFYING THE HEALTH RISKS FROM VERY LOW-DOSE SPARSELY IONIZING RADIATION.

Dreyer NA, Friedlander E
Epidemiology Resources, Inc., P.O. Box 57, Chestnut Hill, MA, 02167
Am J Public Health; 72(6):585-588 1982

11. RISK OF RADIOLOGICAL EXAMINATIONS.

Jankowski J
Instytut Medycyny Pracy w Lodzi, ul. Olowiana 6, 91-614 Lodz, Poland
Pol Przegl Radiol; 45(6):383-386 1981
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12. RADIOBIOLOGY OF RISK ESTIMATES IN MEDICAL IRRADIATION (MEETING ABSTRACT)

Rossi HH
Columbia University, New York, NY
IN: 148th National Meeting of the American Association for the Advancement of Science, January 3-8, 1982, Washington, D.C American Association for the Advancement of Science 182 pp., 1982.

13. RADIATION-INDUCED VASCULAR INJURY AND ITS RELATION TO LATE EFFECTS IN NORMAL TISSUES.

Law MP
MRC Cyclotron Unit, Hammersmith Hosp., London W12 OHS, England
Adv Radiat Biol; 9:37-73 1981

14. CURRENT CONCEPTS IN ULTRAVIOLET CARCINOGENESIS.

Granstein RD, Sober AJ
(c/o Sober) Dept. Dermatology, Massachusetts General Hosp., Boston, MA, 02114
Proc Soc Exp Biol Med; 170(2):115-125 1982

15. METABOLIC CHANGES AFTER EXPOSURE TO RADIONUCLIDES.

Kalistratova VS
No affiliation given
Med Radiol (Mosk); 27(4):62-71 1982
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DIETARY FACTORS IN CARCINOGENESIS

16. CAFFEINE: AN UPDATE.

Oser BL, Ford RA
Bernard L. Oser and Associates, 108-18 Queens Blvd., Forest Hills, NY, 11375
Drug Chem Toxicol; 4(4):311-329 1981

17. ANALYSIS OF MUTAGENIC EFFECTS OF FOREIGN SUBSTANCES IN THE FOOD PRODUCTS.

Maganova NB
Inst. Nutrition, Moscow, USSR
Vopr Pitan; (2):3-8 1982
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EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

18. RADIATION EPIDEMIOLOGY (MEETING ABSTRACT)

Marks S
No affiliation given
148th National Meeting of the American Association for the Advancement of Science, January 3-8, 1982, Washington, D.C. American Association for the Advancement of Science 182 pp., 1982.

19. EPIDEMIOLOGICAL STUDIES ON RADIATION CARCINOGENESIS IN HUMAN POPULATIONS FOLLOWING ACUTE EXPOSURE: NUCLEAR EXPLOSIONS AND MEDICAL RADIATION.

Fabrikant JI
Donner Lab., Univ. California, Berkeley, CA, 94720
Yale J Biol Med; 54(6):457-469 1981

20. EPIDEMIOLOGIC APPROACH TO CANCER.

Guinee VF
Dept. Epidemiology, Univ. Texas System Cancer Center, M.D. Anderson Hosp. and Tumor Inst., Houston, TX
Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.

21. EPIDEMIOLOGY AND EARLY DETECTION OF CANCER OF THE ESOPHAGUS.

Sorouri P
900 Hillside Road, Wilmington, DE, 19807
Gastrointestinal Cancer 1. Decosse JJand Sherlock P, ed. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981.

22. METABOLIC EPIDEMIOLOGY OF LARGE BOWEL CANCER.

Hill MJ
Central Public Health Lab., Colindale Ave., London NW9, England
Gastrointestinal Cancer 1. Decosse JJand Sherlock P, ed. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981.

23. EPIDEMIOLOGY OF GASTRIC CANCER AND ITS PRECURSOR LESIONS.

Correa P
Louisiana State Univ. Medical Center, New Orleans, LA, 70112
Gastrointestinal Cancer 1. Decosse JJand Sherlock P, ed. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981.

24. TRENDS IN THE INCIDENCE OF GASTRIC CARCINOMA (MEETING ABSTRACT)

Nobrega FT
Preventive and Internal Medicine, Mayo Clinic, Rochester, MN
Eleventh Annual William Beaumont Gastrointestinal Symposium, March 24-26, 1982, El Paso, Texas. William Beaumont Army Medical Center 56 pp., 1982.

25. CANCER IN INFLAMMATORY BOWEL DISEASE.

Bayless TM, Yardley JH
Johns Hopkins Hosp., Baltimore, MD, 21205
Gastrointestinal Cancer 1. Decosse JJand Sherlock P, ed. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981.

26. GENETIC ASPECTS OF GUT CANCER.

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Annu Rev Pharmacol Toxicol; 21:133-163 1981

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28. A SEARCH FOR SAFE DRINKING WATER.

Hairstine MA, Schumm HA
Northern Indiana Health Systems Agency, Inc., South Bend, IN
A Search for Safe Drinking Water. Available from National Technical Information Service, Springfield, VA, as HRP-0903845/6:, 68 pp., 1981.

29. OCCUPATIONAL EXPOSURES TO URANIUM: PROCESSES, HAZARDS, AND REGULATIONS.

Stoetzel GA, Fisher DR, McCormack WD, Hoenes GR, Marks S
Battelle Pacific Northwest Lab., Richland, WA
Occupational Exposures to Uranium: Processes, Hazards, and Regulations. Available from National Technical Information Service, Springfield, VA, as PNL-3341-USUR-01:, 91 pp., 1981.

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30. THE ROLE OF RADIATION AND CHEMICALS IN THE INDUCTION OF MUTATIONS AND EPIGENETIC CHANGES DURING CARCINOGENESIS.

Trosko JE, Chang CC
Dept. Human Development, Coll. Human Medicine, Michigan State Univ., East Lansing, MI, 48824
Adv Radiat Biol; 9:2-36 1981

31. SOME EFFECTS OF CARCINOGENS ON CELL ORGANELLES.

Svoboda DJ, Reddy J
Dept. Pathology and Oncology, Univ. Kansas Coll. Health Sciences, Kansas City, KS
Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.

32. CHEMICAL CARCINOGENESIS: INTERACTIONS OF CARCINOGENS WITH NUCLEIC ACIDS.

Rajalakshmi S, Prema M, Sarma D
Dept. Pathology, Univ. Toronto, Toronto, Ontario, Canada
Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.

33. A MOLECULAR RATIONALE FOR NITROSOUREA INDUCED CYTOTOXICITY.

Tew KD
Lombardi Cancer Center, Div. Medical Oncology, Georgetown Univ., 3800 Reservoir Road, N.W., Washington, DC, 20007
INSERM Symp; 19:61-77 1981

34. MODIFICATION OF DNA AND RNA BASES BY THE NITROSOUREAS.

Ludlum DB, Tong WP
Div. Oncology, Dept. Pharmacology and Experimental Therapy, Albany Medical Coll., Albany, NY, 12208
INSERM Symp; 19:21-31 1981

35. CALMODULIN AND CA2+ IN NORMAL AND TRANSFORMED CELLS.

Veigl ML, Sedwick WD, Vanaman TC
Dept. Microbiology and Immunology, Duke Univ. Medical Center, Durham, NC, 27710
Fed Proc; 41(7):2283-2288 1982

36. METABOLISM AND TOXICITY OF AFLATOXINS.

Hsieh DP, Wong JJ
Dept. Environmental Toxicology, Univ. California, Davis, Davis, CA, 95616
Adv Exp Med Biol; 136(partB):847-863 1982

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Lenk W, Scharner U
Pharmakologisches Institut, Universitat Munchen, Nussbaumstrasse 26, D-8000 Munchen 2, W. Germany
Adv Exp Med Biol; 136(partB):951-970 1982

38. METABOLIC ACTIVATION AND DEACTIVATION MECHANISMS OF DI-, TRI-, AND TETRACHLOROETHYLENES.

Henschler D, Hoos R

Inst. Toxicology, Univ. Wurzburg, Versbacher Strasse 9, Wurzburg D-8700, W. Germany

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39. METABOLIC ACTIVATION AND HEPATOTOXICITY OF TRICHLOROETHYLENE.

Reynolds ES, Moslen MT

Chemical Pathology Lab., Dept. Pathology, Univ. Texas Medical Branch, Galveston, TX

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40. THE ACTIVATING ROLE OF GLUTATHIONE IN THE MUTAGENICITY OF 1,2-DIBROMOETHANE.

van Bladeren PJ, Breimer DD, Rotteveel-Smijs GM, Hoogeterp JJ, Mohn GR, De Groot A, Van Zeeland AA, Van der Gen A

Dept. Pharmacology, Univ. Leiden, P.O. Box 9502, 2300 RA Leiden, The Netherlands

Adv Exp Med Biol; 136(partA):809-820 1982

41. METABOLISM OF POLYCYCLIC AROMATIC HYDROCARBONS IN PLACENTA.

Juchau MR, Chao ST, Namkung MJ

Dept. Pharmacology, Sch. Medicine, SJ-30, Univ. Washington, Seattle, WA, 98195

Adv Exp Med Biol; 136(partA):555-573 1982

MODIFICATION OF CARCINOGENESIS

42. THE INTESTINAL ENZYMATIC BIOTRANSFORMATION SYSTEM: POTENTIAL ROLE IN PROTECTION FROM COLON CANCER.

Hoensch HP, Hartmann F

Medizinische Universitatsklinik, D-7400 Tubingen, W. Germany

Hepatogastroenterology; 28(4):221-228 1981

VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

43. THE ONCOGENIC CIRCLE CLOSES.

Rigby PW

Imperial Coll. Science and Technology, London SW7 2BZ, England

Nature; 297(5866):451-453 1982

44. ANALYSIS OF CASES OF HEPATIC CELL CARCINOMA THAT TRANSFORMED FROM VIRAL HEPATITIS.

Ichida F, Homma A, Soga K

Third Dept. Internal Medicine, Niigata Univ. Sch. Medicine, Niigata, Japan

Nippon Rinsho; 40(2):468-477 1982

In JPN

45. ROLE OF VIRUSES IN THE INDUCTION OF PRIMARY INTRACRANIAL TUMORS.

Walsh JW, Zimmer SG, Perdue ML

Div. Neurosurgery, Univ. Kentucky Medical Center, 800 Rose St., Lexington, KY, 40536

Neurosurgery; 10(5):643-662 1982

METHODOLOGY IN CARCINOGENESIS RESEARCH

46. TRANSLATION OF PHARMACOKINETIC/BIOCHEMICAL DATA INTO RISK ASSESSMENT.

Dietz FK, Reitz RH, Watanabe PG, Gehring PJ

Toxicology Res. Lab., Health and Environmental Sciences, Dow Chemical, 1803 Building, Midland, MI, 48640

Adv Exp Med Biol; 136(partB):1399-1424 1982

47. IN VITRO ASSAYS FOR THE DIFFERENTIATION OF TUMOR PROMOTORS FROM CARCINOGENS AFTER ROUTINE CARCINOGENESIS BIOASSAYS (MEETING ABSTRACT)

Ward JM, Rice JM

Frederick Cancer Research Center, Frederick, MD

Second Annual Meeting of the Society of Environmental Toxicology and Chemistry, November 22-25, 1981, Arlington, Virginia. Society of Environmental Toxicology and Chemistry 150 pp., 1982.

48. ENVIRONMENTAL CARCINOGENS: SELECTED METHODS OF ANALYSIS. VOLUME 4. SOME AROMATIC AMINES AND AZO DYES IN THE GENERAL AND INDUSTRIAL ENVIRONMENT.

Egan H, Fishbein L, O'Neill IK, Castegnaro M, Bartsch H

Lab. Government Chemist, London, England

IARC Sci Publ (40): 347 pp., 1981.

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DECEMBER, 1982

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PREVALENCE OF GI CANCER IN HUMAN POPULATIONS

1. EPIDEMIOLOGY OF ESOPHAGEAL CANCER IN SAO PAULO, BRASIL.

Mirra AP, Pacheco de Souza JM, Gotlieb SL, Pastorelo EF, Bussacos MA, Da Motta Azevedo Correa MC, Haenszel W, Correa P
Departamento de Epidemiologia da Faculdade de Saude, Registro de Cancer de Sao Paulo, USP, Av. Dr. Arnaldo, 715, 01255 Sao Paulo, Brasil

Rev Saude Publica; 16(1):54-65 1982

The incidence by age, sex and birthplace of esophageal cancer in Sao Paulo in 1975 was compared with that of 1969, in the rest of Brasil and other countries. The Cancer Registry shows that of the 243 recorded cases of esophageal cancer in Sao Paulo in 1975, 200 were males and 43 were females. This is a male:female incidence ratio of 4.6. The other major Brazilian cities, Recife, Rio Janeiro and Fortaleza have a lower male:female incidence ratio: ranging from 1.6 to 3.3. The increased immigration into Sao Paulo from Portugal, Italy, Spain and Japan could contribute to this significant difference between Brazilian cities. The male:female ratio remains high for native citizens of Sao Paulo when birthplace is considered al-

HE 20. 3173/2:

though the incidence rate is less overall for natives vs immigrants. There is a higher risk for immigrants to Sao Paulo of contracting esophageal cancer than for locally born citizens. This is also linked to age, those over 50 yr old, and sex, higher for males, for natives as well as immigrants. Therefore, the etiology can not be a general one of social structure, stress or malnutrition among immigrants. The increased risk factor for Sao Paulo as compared to the rest of Brasil and in some other countries must be due to something specific to the city of Sao Paulo. Future Cancer Registry information will include the date of arrival and length of stay in the city for immigrants and the exact birthplace for each cancer patient. (15 Refs) (In POR)

2. THE EPIDEMIOLOGY OF CANCER IN CHINA.

Armstrong B
Dept. Medicine, Univ. Western Australia, Queen Elizabeth II Medical Centre, Nedlands, Western Australia, Australia
World Health Forum; 3(1):95-101 1982

Epidemiology of cancer in China based on a retrospective survey of cancer mortality with additional data on the main cancer sites is reviewed. A total of 18,439,072 deaths were surveyed and 1,868,310 (10.1-11.3% in males and 8.8% in females) were attributed to cancer. The highest level of diagnosis and treatment and the best available criterion for the diagnosis of cancer are summarized. For all sites of cancer together the estimated mortality rates in China were 119.6/100,000 for males and 80.7/100,000 for females, adjusted to age distribution of the 'world' population. Among countries reporting mortality by site of cancer, China has the highest mortality from esophageal cancer with annual rates of 31.7/10,000 in males and 15.9/100,000 in females. Cancer of the stomach is the most common form of cancer leading to death in China. The mortality rates are 32.4 and 15.9/100,000 in males and females, respectively. The rates are substantially lower than those in Japan. Liver cancer (presumed primary) is the third more important cancer as a cause of death in China and accounts for 15% of all cancer deaths. Mortality rates of the cancer of the cervix are generally higher in the rural than in urban areas. An unusual feature of the high rate of lung cancer in Chinese women, particularly Cantonese women, is the relatively high proportion of the tumors which are adenocarcinomas. The county with highest rates of large bowel cancer is an area of endemic schistosomiasis in Zhajiang province. The geographic distribution of nasopharyngeal cancer within China is quite remarkable, with a very high incidence area centered on Guandong province in the south. (11 Refs)

3. TREND IN TUMOR INCIDENCE AND POSSIBLE RELATION TO CANCER SCREENING.

Neumann G
Hohe Strasse 28, D-7000 Stuttgart 1, W. Germany
Fortschr Med; 100(23):1073-1078 1982

Trends in incidences of various malignant tumors and their relation to participation in screening programs are discussed with emphasis on the current situation in the Federal Republic of Germany. In general, absolute numbers of cancer cases are increasing as the result of changes in the age-distribution of the general population. The incidence of lung cancer is increasing, while that of gastric cancer is decreasing. In industrial nations the mortality due to intestinal, rectal, and prostatic cancers among men is rising. Among women, the incidences of uterine and gastric cancers are decreasing, while those of lung and breast cancers are increasing; trends in incidences of rectal and intestinal cancers are not uniform. Participation in screening programs generally correlates inversely with mortality. Participation is highest among age groups with low incidences of cancer; screening therefore has limited effect on the epidemiology of cancer. In one period the mortality due to colon, rectum, breast, or prostate was higher than expected in spite of cancer screening. In contrast, cervical cancer mortality was lower than would be expected from screening. Because the site of many uterine cancers is not recorded, mortality rates for cervical cancer are not very useful. (20 Refs) (In GER)

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN GI CARCINOGENESIS

4. MORTALITY AMONG RUBBER WORKERS: V. PROCESSING WORKERS.

Delzell E, Monson RR
Duke Univ. Comprehensive Cancer Center, Durham, NC
JOM; 24(7):539-545 1982

Cause-specific mortality was evaluated among 2,666 men employed in the processing division of a rubber manufacturing plant. The division was divided into two sections: front processing (compounding, mixing and milling operations) and back processing (extrusion, calendering, cement mixing and rubberized fabrics operations). Mortality rates for all processing workers combined and for men in each section were compared with rates for US white males or for workers employed in other divisions of the same plant. Compared with either referent group, men in the processing division had increased mortality from leukemia, emphysema, and cancers of the stomach, large intestine, and biliary passages and liver. An excess number of deaths from stomach and large intestine cancer was found predominantly among men in the front processing section (33 observed vs 17.7 expected deaths, based on rates in nonprocessing workers). Increased mortality from leukemia (14 observed vs 7.3 expected) and from emphysema (22 observed vs 11.0 expected) was present among men employed in the back processing section. Examination of mortality from these causes according to age and the yr starting work, duration of employment, and yr since starting work in the relevant sections of the processing division suggested that observed excesses of stomach cancer, large intestine cancer, leukemia, and emphysema among processing workers are related to occupational exposures. These results are consistent with the findings of studies of other groups of rubber workers. (Author abstract) (20 Refs)

5. IARC MONOGRAPHS ON THE EVALUATION OF THE CARCINOGENIC RISK OF CHEMICALS TO HUMANS: THE RUBBER INDUSTRY.

IARC Working Group
Div. Environmental Carcinogenesis, International Agency for Res. on Cancer, Lyon, France
IARC Monogr Eval Carcinog Risk Chem Hum 28: 486 pp., 1982.

The carcinogenic risks of exposures to workers in the rubber industry is evaluated. Manufacturing of tires, and other rubber goods are considered with respect to exposures incident to the mixing of elastomers with chemicals and their subsequent conversion into finished products. An historical overview is presented with discussion of the origins of the rubber industry and the developing rubber industry and its occupational health hazards. Manufacturing processes are described for tires, tubes, remolds, and retreads; general rubber goods such as wire and cables, belting, hose, ebonite, rubber footwear, food processing equipment, aircraft deicing equipment, automobile parts; proofed rubber fabrics, adhesives and sealants; and dipped latex products and forms. The chemistry of rubber compounding is reviewed. Exposures in the workplace are discussed with respect to controls, protective equipment, work practices; studies of exposures in the workplace; and biological monitoring. Biological effects include carcinogenic, mutagenic, and teratogenic effects of exposure to accelerators, antioxidants, curing agents; solvents; monomers; talc; carbon blacks; aromatic amines; mineral oils, tar products and polycyclic aromatic hydrocarbons; nitroso compounds; phthalate and adipate esters; and curing fumes and other emissions. Effects in humans other than cancer including dermatologic respiratory, and reproductive, are discussed. Epidemiological studies of carcinogenicity in humans are reviewed: definite associations with cancer of the urinary bladder, lymphatics, stomach, lung, and perhaps, other sites, have been made. (367 Refs)

6. MORTALITY AMONG WORKERS IN A NICKEL REFINERY AND ALLOY MANUFACTURING PLANT IN WEST VIRGINIA.

Enterline PE
Dept. Biostatistics, Graduate Sch of Public Health, Univ. Pittsburgh, Pittsburgh, PA, 15261
JNCI; 68(6):925-933 1982

Workers from a nickel refinery at Huntington, W. Va., which received a nickel matte from smelters in Onatrio, Canada, during 1922-47 were studied for excesses in sinonasal and lung cancers. Other workers who were in a nickel alloy production plant operated in conjunction with the refinery but who did not work in the refinery were also studied. Evidence is presented on the existence of a nasal cancer hazard and possibly a lung cancer hazard among workers employed in the nickel refinery. Two of these workers developed a sinonasal cancer. Evidence of a respiratory cancer hazard in other parts of the plant before or after 1947 is weak, and the observed results could be due to chance variations from the mortality experience of the standard reference populations. Among nonrefinery workers hired while the nickel refinery was in operation, 2 employees had a probable sinonasal cancer. The first employee worked in a high-temperature conversion process where nickel carbonate was decomposed to nickel oxide, and the second employee is believed to have done maintenance work in the plant where this process was used. For both cohorts combined there were slight overall excesses in lung, stomach, and prostate cancers with some evidence of a dose-response relationship for these cancers. (Author abstract) (11 Refs)

DIETARY AND DIGESTIVE FACTORS IN GI CARCINOGENESIS

7. RELATIONSHIP OF DIET TO THE INCIDENCE OF ESOPHAGEAL AND STOMACH CANCER IN JAPAN.

Nagai M, Hashimoto T, Yanagawa H, Yokoyama H, Minowa M
Dept. Public Health, Jichi Medical Sch., Tochigi-ken, Japan
Nutr Cancer; 3(4):257-268 1982

The food intake of households in 1,040 census tracts sampled in 1974, 1975, and 1976 for the nationwide nutrition survey of the Japanese Ministry of Health and Welfare, and the standardized mortality ratios (SMRs) of stomach and esophageal cancers from 1969 to 1974 for the cities, towns, and villages of the nutrition survey areas, were linked and their relationship was observed statistically by correlation analysis and multiple regression analysis. The results obtained are summarized as follows: (1) The food items positively related to the SMR for stomach cancer were wheat, pickled vegetables, and beef, while tofu (soybean curd) was negatively related. (2) Foods positively related to esophageal cancer were wheat, pork, and dried or salted fish. (3) Pickled vegetables and dried or salted fish contain a high percentage of salt (NaCl), and thus the positive relationship of these foods to both stomach and esophageal cancers suggests a relationship between salt and these diseases. (Author abstract) (8 Refs)

8. RELATIONSHIP OF SOYBEAN PASTE SOUP INTAKE TO GASTRIC CANCER RISK.

Hirayama T
Epidemiology Div., Natl. Cancer Center Res. Inst., 1-1, Tsukiji 5-chome, Chuo-ku, Tokyo, 104, Japan
Nutr Cancer; 3(4):223-233 1982

Daily intake of soybean paste soup was found to significantly reduce standardized mortality rates for gastric cancer in an ongoing large-scale prospective study of 122,261 males and 142,857 females aged 40 and above in 29 Japanese health center districts, 1966-1978. The gastric cancer standardized mortality rates were 171.9, 210.2, 240.0, and 255.9 per 100,000 males, and 77.8, 85.3, 97.5, and 113.6 per 100,000 females in daily, occasional, rare, and noningesters, respectively. These relationships remained significant when observed by age group, district, socioeconomic status, dietary pattern, and smoking habit. The risk-reducing effect has also been observed in case-control studies in the past, for both males and females and in urban and rural areas. This beneficial effect could arise from selected compounds such as protease inhibitors and/or other nutritious substances included in the soybean, but it is also possible that it merely reflects the effect of some frequent accompaniment to soybean paste soup, such as green-yellow vegetables. (Author abstract) (16 Refs)

9. CANCERS OF THE DIGESTIVE TRACT, ALCOHOL AND TOBACCO.

Tuyns AJ, Pequignot G, Gignoux M, Valla A
International Agency for Res. on Cancer, 150, cours A. Thomas, 69372 Lyon Cedex, France
Int J Cancer; 30(1):9-11 1982

In a systematic search for risks associated with the consumption of alcohol and tobacco in relation to cancers of the digestive tract, esophageal cancer was found to be significantly related to both factors. There was a slightly elevated risk for rectal cancer among alcohol consumers as well as a lower risk for gastric cancer. With the exception of esophageal cancer, none of the other digestive tract cancers were found to be associated with tobacco consumption. (Author abstract) (17 Refs)

10. ALCOHOL AND CARCINOGENESIS.

Seitz HK, Czygan P, Kommerell B
Schwerpunkt Gastroenterologie, Medizinische Universitatsklinik, Bergheimer Str. 58, D-6900 Heidelberg 1, W. Germany
Leber Magen Darm; 12(3):95-107 1982

The relationship between alcoholism and carcinogenesis is reviewed. Alcohol has been linked to increased incidences of cancers of the oropharynx, larynx, esophagus, liver, and probably the pancreas and rectum. Beverages with high alcohol content present greater risks than wine or beer. Alcoholism has a synergistic effect on carcinogenesis caused by smoking. Cirrhosis of the liver caused by alcoholism is important as a precancerous condition. Beer consumption increases the risk of pancreatic cancer; chronic pancreatitis is not involved as an intermediate stage. Beer consumption also increases the incidence of rectal cancer. Other cancers possibly related to alcohol abuse include carcinomas of the kidney, prostate, bladder, breast, and thyroid. Animal studies indicate that alcohol by itself is not carcinogenic. Alcohol apparently has a cocarcinogenic effect. Alcohol may induce specific enzyme systems that interact with carcinogens. It may be active in either the initiation phase, the promotion phase, or both. In the gastrointestinal tract it may induce carcinogenesis by local effects. Systemic effects include alterations in hormonal and immune functions, as well as in the actions of vitamins and minerals. In addition, alcoholic beverages contain a number of carcinogenic substances. (179 Refs) (In GER)

11. EFFECT OF BILE ACIDS ON 1,2-DIMETHYLHYDRAZINE-INDUCED COLON CANCER IN RATS.

Koga S, Kaibara N, Takeda R
Dept. Surgery, Tottori Univ. Sch. Medicine, Yonago-shi, Nishi-machi 36-1, Tottori 683, Japan
Cancer; 50(3):543-547 1982

The effects of intercepting a part of the enterohepatic circulation of bile acids by ileal resection or bypass on the quantitative and qualitative changes of fecal bile acids were investigated in rats, and the relationship of these changes to the development of DMH-induced colon cancer was studied. The daily fecal total bile acid level was increased in all intercepted groups, especially those with long resection and exclusion. Total bile acid levels played a greater role in the development of DMH-induced colon cancer than did primary or secondary bile acid levels individually. Our findings suggest that bile acid acts as a promoter in the development of colon cancer. (Author abstract) (19 Refs)

12. THE PHYSIOLOGICAL IMPORTANCE OF THE COLONIC MICROFLORA.

Gustafsson BE
Dept. Germfree Res., Karolinska Inst., Box 60 400, S-104 01 Stockholm, Sweden
Scand J Gastroenterol [Suppl]; 17(77):117-131 1982

The present concept of the intestinal microflora has been reviewed with stressing the fact that it represents an entity with a wt comparable to one of the large organs of the body. It is composed of about 500 different strains, many of which as yet have not been isolated because 95% of them are anaerobic and fastidious in their growth requirements. The intimate relationship of the flora to the surface epithelium of the intestines and the Lieberkuhn's crypts are brought forward. The production of germfree animals is reviewed as an accounting of the most obvious differences between the germfree animal and its conventional counterparts, as far as gastroenterology is concerned. This includes the protective function of the normal intestinal flora, the cecum enlargement in germfree rodents, the influence of the flora on the metabolism of bilirubin, intestinal mucin, and pancreatic enzymes. Differences found in germfree animals due to the absence of the microbial flora related to the metabolism of fatty acids, bile acids, cholesterol and steroid hormones are also reviewed. The germfree animal has even proven to be an important research tool in such fields as carcinogenesis and studies of Crohn's disease and ulcerative colitis. There is need of a wider use of the germfree animal as a baseline in studies on the interference of the intestinal microbial flora with factors and conditions of great physiological and clinical importance. (Author abstract) (101 Refs)

13. HOW TO PREVENT CANCER OF STOMACH AND COLON: SMALL MICROBES ARE BIG PRODUCERS OF CARCINOGENS.

Stortebecker P
Akerbyvagen 282, S-183 35 Taby/Stockholm, Sweden
How to Prevent Cancer of Stomach and Colon: Small Microbes are Big Producers of Carcinogens. Stockholm, Stortebecker Foundation for Research, 72 pp., 1981.

Colon cancer is not caused by carcinogens supplied by the food or intake of beverages, but is the result of local production of carcinogens in the colon itself. Stomach cancer may to some degree be caused by an exogenous supply of carcinogens through ingestion, although, stomach cancer is predominantly due to an endogenous production of carcinogens within the gastric contents. Relevant cancer-causing factors of stomach and colon cancer are reviewed. Cancer epidemiology is outlined, and normal functions of the digestive tract are reviewed. Causes of stomach cancer may include physicochemical injuries to gastric mucosa (hot food and beverages, tannic acid from black coffee and tea, alcohol), exogenous carcinogens (broiled foods, nitrosamines, mycotoxins, pickled cabbage and Geotrichum candidum, Japanese soya and sake), and endogenous carcinogen production. Colon cancer is discussed with respect to the production of microbes, gastrointestinal cancer, transit time, diet, and disorders with a predisposition to colon cancer (chronic ulcerative colitis, polyps and polyposis of the colon). Stomach cancer may be prevented by avoidance of physicochemical injuries and the addition of glutamic acid hydrochloride to persons with achlorhydria in order to restrain microbial growth. Colon cancer can be prevented by maintaining a rapid transit time within the intestine in order to avoid production and retention of microbial carcinogens within the body. (60 Refs)

14. FECAL NEUTRAL AND ACID STEROIDS AND B-GLUCURONIDASE AND 7ALPHA-DEHYDROXYLASE ACTIVITIES IN COLON CANCER AND CONTROL SUBJECTS (MEETING ABSTRACT).

Hathaway L, Ross JK, Leklem E
University of Vermont, Burlington, VT, 05405
Fed Proc; 41(3):354 1982

Neutral (NA) and acid (AS) steroids and 7 alpha-dehydroxylase (7alpha) and B-glucuronidase (BG) activities were determined in feces of 4 colon cancer patients, mean age (MA) 62 years and 6 controls, MA 49 years. For cancer patients, BG was 83 units/mg protein/hr and 7 alpha activity measured by production of deoxycholate (DCA) 11.9 and lithocholate (LCA) 2.1 nm/mg protein/hr. Controls had 201 units of BG and 5.7 nm DCA and 1.4 nm LCA for 7 alpha. While mean DCA and LCA levels of cancer subjects were higher than the controls as expected from other research, the differences were not significant due to wide individual variation. Certain changes in dietary fat and fiber are known to alter NS, AS, BG, and 7 alpha. Eighteen male controls (MA equals 24) on a test diet containing 2424 Cal, 81 g protein, 93 g fat, 720 mg cholesterol, and 3.6 g neutral detergent fiber were compared with 10 male and female controls (MA equals 27) on self-selected (SS) diets. For the test diet, mean total NS was 27.3 and mean total AS 13.3 mg/g dry wt feces. SS diets had mean total NS of 18.5 and mean total AS of 11.1 mg/g dry wt. Enzymes, quantified for 7 subjects on the test diet were 166 units of BG and 21.3 nm LCA and 12.3 nm LCA for 7 alpha. For SS diets BG was 151 units and 7 alpha was 23.3 nm for DCA and 8.1 nm for LCA. Only NS was significantly different between the diet groups. (no Refs)

OTHER ETIOLOGIC FACTORS IN GI CARCINOGENESIS

15. GASTRITIS AS A RISK FACTOR IN CARCINOGENESIS: EPIDEMIOLOGICAL AND MORPHOLOGICAL FINDINGS.

Heilmann KL, Cuello C, Hoepker WW
Pathologisches Institut, Stadtische Krankenhaus Landshut, Robert-Koch-Str. 1, D-8300 Landshut, W. Germany
Leber Magen Darm; 12(3):115-121 1982

Gastric biopsies were performed on 239 persons from the district of Narino in Columbia. This district has an incidence of gastric cancer of 150/100,000, compared with an incidence of 40/100,000 in West Germany. Age and sex were determined for 159 of the persons and results of biopsies for these persons were compared with those for 159 Germans who were matched for age and sex. None of the persons selected for study had gastric cancer. The age-groups most represented were the 41-50-yr-old group for men and the 31-40-yr-old group for women. Gastritis without atrophy was found in 53% of the high-risk Columbian group and in 76% of the low-risk German group (controls). Atrophic gastritis of the antrum was found in 46% of the high-risk group and in 23% of the controls. Among patients with gastritis of the corpus, nonatrophic gastritis predominated in both groups; atrophic gastritis was present in 14% of the high-risk group and in 4% of the controls. The incidence of atrophic gastritis was independent of age in both groups. Histologic examination showed necrosis in the glandular neck region in 122 of the test subjects; 83.6% of these were high-risk patients and 16.4% were controls. Hyperplasia of the glandular neck region was found in 212 subjects, of whom 65% were high-risk and 34% were controls. Dysplastic changes occurred in 45% of the subjects studied, of which 88% were high-risk. Intestinal metaplastic lesions were found in 100 high risk patients and in 39 of the controls. Hyperplastic forms of metaplasia were found in 65 patients, of whom 80% were high-risk. The findings suggested that active, progressive gastritis may be a preliminary stage of the intestinal ('epidemiological') type of gastric carcinoma. (19 Refs) (In GER)

16. NATURAL HISTORY OF HEREDITARY CANCER OF THE BREAST AND COLON.

Albano WA, Recabaren JA, Lynch HT, Campbell AS, Mailliard JA, Organ CH, Lynch JF, Kimberling WJ
Inst. Familial Cancer Management and Control Incorporated, 2500 California, Omaha, NE, 68178
Cancer; 50(2):360-363 1982

The natural history of 106 patients from 18 families manifesting hereditary breast cancer syndromes, and 117 affected patients from 20 families manifesting nonpolyposis hereditary colon cancer were evaluated. Findings were compared with the American College of Surgeons (ACS) long-term audits for breast and colon cancer respectively. The cardinal features of hereditary cancer were observed within the study group, including: (1) a significant younger age of onset (49 years, breast; 46 yr, colon); (2) an excess of proximal lesions in the hereditary colon series (49%); and (3) an excess of bilaterality in the hereditary cancer patients. The clinical stage at presentation was similar for the hereditary and ACS audit patients. Five-yr survival was significantly improved (p less than 0.05) for both hereditary cancer populations are compared to the ACS audits (67% hereditary breast cancer and 52% nonpolyposis hereditary colon cancer). Improved survival in hereditary colon and breast cancer patients may have a bearing on the design of future clinical protocols. (Author abstract) (15 Refs)

17. MALIGNANCIES AND EXPOSURE OF THE YOUNG TO IONIZING RADIATION.

Schull WJ, Kato H

Center for Demographic and Population Genetics, Univ. Texas Health Science Center at Houston, Houston, TX

Cancer Bull; 34(3):84-89 1982

Risk of radiation-related malignancies in individuals exposed in the first two decades of life in Hiroshima and Nagasaki is described. The relative risk of death due to leukemia in the 'heavily' exposed, particularly among those individuals exposed in the first decade of life, is much higher than the relative risk for exposures at subsequent ages. For the three most common radiation-related malignancies, cancers of breast, lung, and stomach, the absolute risk of death, for age-at-death specific groups, is higher the younger the age at the time of the bombing (ATB). Carcinoma of the thyroid was diagnosed during life more commonly in persons who were less than 20 yr of age ATB. The excess incidence of the malignancy/10(6) person-yr-risk/rad was 2.1, 2.3, 0.33, 0.28, and-0.07 for exposures at less than 10, 10-19, 20-34, 35-49, and 50 or more yr of age ATB, respectively. A study of 339 fatal and nonfatal malignancies among young survivors in the period 1950-1974 demonstrated that aside from the increased frequency, the distribution of malignant solid tumors differed little from that seen among individuals who were 20 yr of age or older when exposed. The diminished risk of radiation-related breast cancer among females exposed in the circum-menopausal years suggests that the endocrinologic status and possibly other factors may influence this specific risk. Whether the increased risk extends uniformly to all exposed individuals or whether there are especially vulnerable, 'high-risk' persons, is unknown. (26 Refs)

18. DOES THE POLYP CANCER SEQUENCE APPLY TO THE DUODENUM?.

Widgren S

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Praxis; 71(21):907-910 1982

The link between dysplasia, adenoma, and carcinoma of the duodenum is discussed based on the finding of four duodenal adenocarcinomas with components of tubular or tubular/villous adenomas. Histological characteristics of the benign and malignant components are described. Existence of areas of moderate or severe dysplasia in certain adenomas of the duodenum, and of tubular and villous structures in malignant duodenal lesions suggests the adenoma-carcinoma sequence. (6 Refs) (In FRE)

INDUCTION OF GI CARCINOGENESIS IN ANIMALS

19. GASTRIC CARCINOGENESIS BY 4-(HYDROXYMETHYL)BENZENEDIAZONIUM ION(TETRAFLUOROBORATE) OF AGARICUS BISPORUS (MEETING ABSTRACT).

Toth B

Eppley Institute for Research in Cancer and Allied Diseases, Omaha, NE, 68105

Proc Am Assoc Cancer Res; 23:196 1982

The aim of this investigation was to explore the tumor-inducing effect of a single oral administration of 4-(hydroxymethyl)benzenediazonium ion(tetrafluoroborate)-(4-HMBD) of the cultivated mushrooms of commerce Agaricus bisporus. For this reason, a single intragastric instillation of 400 ug 4-HMBD per g of body weight was given to Swiss albino mice. As a solvent control, sodium tetrafluoroborate (STB) was administered by the same method as above to another group of mice. Each group consisted of 100 animals. As a result of treatment, 29% of the females (3 are still living) and 28% of the males developed glandular stomach tumors, while none were observed in the solvent-instilled control groups. Histopathologically, the tumors were classified as polypoid adenomas and adenocarcinomas. This diazonium ion was detected in the aqueous extract of Agaricus bisporus at a level of 0.6 ppm. In addition, it was revealed that the ion is generated from the agaritine component of this mushroom by an enzyme system acting in situ. An earlier investigation demonstrated that when given subcutaneously to mice, 4-HMBD induced tumors of the subcutis and skin. Since the human population consumes large amounts of Agaricus bisporus, the findings carry practical environmental implications. (1 Ref)

20. HYPERPLASIA AND HYPERPLASTIC POLYPS IN THE LARGE INTESTINE OF MICE DURING 1,2-DIMETHYLHYDRAZINE-INDUCED CARCINOGENESIS.

Krutovskikh VA

All-Union Cancer Res. Center, Moscow, USSR

Eksp Onkol; 4(3):20-25 1982

Development and potential malignant transformation of hyperplastic polyps of the large intestine were studied in male (CBA x C57BL)F1 mice exposed to 1,2-dimethylhydrazine (DMH: 16 mg/kg/wk, sc). Within different time periods after the initiation of DMH administration, the mice were sacrificed, and specimens of large intestine were subjected to scanning electron microscope examination. The DMH administration resulted in progressive changes in the ultrastructure of crypts. Hyperplastic exophytic nodules were first detected 10-15 wk after the initiation of the experiment. The number of nodules correlated with the degree of hyperplasia of the intestinal mucosa. Approx 5-10% of the hyperplastic polyps showed malignant transformation; spherical or saucer-like tumors with foci of tissue atypia were first detected after 20-wk administration of the DMH. All tumors observed after 25-30-wk administration infiltrated the intestinal wall. (14 Refs) (In RUS)

21. PERIANAL LESIONS OF BALB/C MICE INDUCED BY 1,2-DIMETHYLHYDRAZINE DIHYDROCHLORIDE AND METHYLAZOXYMETHANOL-ACETATE: THEIR CLASSIFICATION AND HISTOGENESIS.

Kumagai H, Kawaura A, Furuya K, Izumi K, Otsuka H
Second Dept. Pathology, Sch. Medicine, Univ. Tokushima, Kuramoto-cho 3-18-15, Tokushima 770, Japan
Gan; 73(3):358-364 1982

The histogenesis of perianal squamous cell carcinomas induced by subcutaneous and intraperitoneal injection of 1,2-dimethylhydrazine dihydrochloride (DMH) and painting of methylazoxymethanol (MAM)-acetate on the anal region was investigated in 212 female BALB/c mice. Painting of MAM-acetate and injection of DMH induced similar benign and malignant tumors and hyperplastic lesions in the anal region. In chronological studies on animals given DMH subcutaneously, cystic or solid squamous lesions, foci of immature sebocytes, sebaceous hyperplasias and sebaceous adenomas were identified. These lesions seemed to be precursors of carcinomas that developed in the same region, and originated from hair follicles or sebaceous glands of the pilosebaceous complexes, but not from the anal mucosa. In mice treated with DMH, the incidence of perianal carcinomas was high in groups with high incidences of colon carcinomas. (Author abstract) (18 Refs)

22. INDUCTION OF STOMACH CANCER IN EXPERIMENTAL ANIMALS BY CHEMICAL CARCINOGENS (MEETING ABSTRACT).

Preussmann R
Institut fur Toxikologie und Chemotherapie, Im Neuenheimer Feld 280, D 6900 Heidelberg, W. Germany
J Cancer Res Clin Oncol; 103(Suppl):A10 1982

A survey on the induction of gastric cancer in experimental animals by chemical carcinogens shows that especially those carcinogens are important which act 'locally' and do not need enzymatical activation. Several N-nitrosamides have been used as model substances for the induction of stomach cancer. They induce selectively and in high incidences tumors of the glandular stomach as well as of the forestomach in small rodents. Structure-effect relationships as well as differences in the species will be discussed. Methyl-nitrosonitroguanidin (MNNG) has been shown to be the standard carcinogen for the induction of gastric cancer in higher developed species eg dogs, or rodents. (no Refs)

23. CARCINOGENESIS BY ISOMERS OF N-NITROSO-3,5-DIMETHYLPIPERIDINE.

Lijinsky W, Reuber MD, Singer SS, Singer GM
Chemical Carcinogenesis Program, NCI-Frederick Cancer Res. Facility, Frederick, MD, 21701
JNCI; 68(6):989-991 1982

The cis- and trans-isomers of N-nitroso-3,5-dimethylpiperidine were administered separately in drinking water solution to groups of 20 female F344 rats for 50 weeks. The concentrations of the solutions were 0.72 mM for the cis-isomer and 0.14 mM for the trans-isomer. In both groups the animals died with tumors of the upper gastrointestinal (GI) tract, mainly carcinomas of the esophagus, at about the same time. A third group of animals was given a mixture of the two isomers in the ratio of 5 cis:1 trans, and these animals died more rapidly with the same upper GI tumors. The trans-isomer appeared to be a more potent carcinogen than the cis-isomer. The 3,5-dimethyl derivative is a less potent carcinogen than nitrosopiperidine. (Author abstract) (8 Refs)

24. DOSE-RESPONSE FOR BENZO(A)PYRENE METABOLITE-DNA ADDUCTS IN LUNG, LIVER, AND FORESTOMACH OF MICE (MEETING ABSTRACT).

Anderson MW, White CM, Adriaenssens PI
National Institute of Environmental Health Science, Research Triangle Park, NC, 27709
Fed Proc; 41(3):1548 1982

The formation of benzo(a)pyrene (BP) metabolite-DNA adducts in lung, liver, and forestomach of female A/HeJ mice was examined as a function of BP dose (po) ranging from 2 to 1350 umol/kg. The major identified adduct in each tissue at each dose was the 7beta,8alpha-dihydroxy-9alpha,10alpha-epoxy-7,8,9,10 tetrahydro-BP (BPDEI)-deoxyguanosine adduct. The 7beta,8alpha-dihydroxy-9beta,10beta-epoxy-7,8,9,10 tetrahydro-BP(BPDEII)-deoxy guanosine adduct and a BP-phenol-oxide-DNA adduct were also observed. The dose-response curves for these adducts were sigmoidal in each tissue. The DNA binding expressed as percentage of exposure dose was largest at a BP dose of 0.3 mmol/kg. The dose-response relationships approached linearity at low doses. Thus, the results of these dose-response studies do not reveal the existence of any threshold dose below which binding of BP metabolites to DNA does not occur. Dose-response curves for binding of BP metabolites to protein were also investigated. The ratio of BPDE-DNA adduct levels to protein binding levels was non-linearly related to exposure dose. Thus, binding of BP metabolites to protein cannot be used as a gauge of BP metabolite-DNA binding. These and similar dose-response relationships for polycyclic aromatic hydrocarbons (PAH) metabolite-DNA adducts should be helpful in the low dose extrapolation problem for PAH carcinogenesis. (no Refs)

25. SPONTANEOUS COLON ADENOCARCINOMA IN THE COTTON-TOP TAMARIN, SAGUINUS OEDIPUS OEDIPUS, AS A MODEL FOR HUMAN COLON CANCER (MEETING ABSTRACT).

Clapp NK, Lushbaugh C, Tankersley WG, Gangaware BL, Humason GL
Medical and Health Sciences Division, Oak Ridge Associated Universities, Oak Ridge, TN, 37830
Proc Am Assoc Cancer Res; 23:416 1982

Investigation of experimental colon cancer has been greatly enhanced by synthesis of 1,2-dimethylhydrazine (DMH) and its metabolites. However, until the recognition of spontaneous colon cancer in Saguinus oedipus oedipus, no model of spontaneous occurrence of the disease had been identified in experimental animals where incidence was high enough to enable study of causal factors. In our colony, fifty-three animals have now died since 1968 with 1 or more colonic mucinous adenocarcinomas, characterized by early metastases, no difference in sexual sensitivity and occurrence in both imported and colony-born animal. Mean ages of occurrence are: for import males, 49.5 mos, females, 52.5 mos; for colony-bred males, 45.5 mos, females, 32.2 mos. The tumor is age dependent; the shortest colony time for tumor expression has been 4 mos, and no tumor has been observed in animals living beyond 7 years colony time. Numbers of large bowel tumors were: cecum-23, ascending-22, transverse-14, descending colon-25, and rectum-9. The high incidence of spontaneous colon cancer in S oedipus oedipus and total absence of this cancer in several hundred Saguinus fuscicollis tamarins and Callithrix jacchus marmosets from our colony suggest a strong genetic-related susceptibility. Ongoing comparisons of basic biochemical and microfloral fecal changes of susceptible with nonsusceptible species should provide some insight into possible physiological differences between the species which may contribute to cancer induction and may relate to human colon cancer occurrence. (no Refs)

MECHANISMS AND MODIFICATIONS OF GI CARCINOGENESIS

26. COMBINED INHIBITORS OF CARCINOGENESIS: EFFECT ON AZOXYMETHANE-INDUCED INTESTINAL CANCER IN RATS.

Nigro ND, Bull AW, Wilson PS, Soullier BK, Alousi MA
Dept. Surgery, Wayne State Univ. Sch. Medicine, 540 East Canfield Ave., Detroit, MI, 48201
JNCI; 69(1):103-107 1982

Outbred male Sprague-Dawley CD rats were fed complete semisynthetic diet and were given supplemental low doses (2 ppm) of selenium as H_2SeO_3 in their drinking water or 50 mg 13-cis-retinoic acid (13-cis-RA) and 2 g beta-sitosterol/kg diet either singly, in combinations of two, or in combinations of all three. Intestinal tumors were induced with eight weekly sc injections of 8 mg azoxymethane (ACM)/kg body weight, and inhibition of tumor formation was determined by tumor counts after 26 weeks. Noncarcinogen controls for each dietary group received eight injections of sterile water. Tumor inhibition was statistically significant in two groups of animals: Dietary control animals had a tumor frequency of 5.07 tumors/rat, rats receiving selenium- plus 13-cis-RA supplementation had a tumor frequency of 3.77, and those being given the combination of all three inhibitors had 2.75 tumors/rat. Analysis of fecal steroids from three AOM groups (dietary controls, the beta-sitosterol plus 13-cis-RA-supplemented group, and the group receiving all 3 additives) after 4 months of supplementation showed that the addition of beta-sitosterol to the diet had no effect on acidic or neutral steroids, regardless of the observed difference in tumor frequency. These results suggest that subpharmacologic doses of inhibitors, particularly those that inhibit the process by different mechanisms, while ineffective alone, may provide significant inhibition of tumorigenesis when used in combination. (Author abstract) (21 Refs)

27. INHIBITION OF DEVELOPMENT OF METHYLNITROSOUREA-INDUCED RAT COLONIC TUMORS BY PERORAL ADMINISTRATION OF INDOMETHACIN.

Narisawa T, Sato M, Sano M, Takahashi T
Dept. Surgery, Akita Univ. Sch. Medicine, Hondo 1-1-1, Akita 010, Japan
Gan; 73(3):377-381 1982

The nonsteroid antiinflammatory drug indomethacin, a prostaglandin synthesis inhibitor, inhibited the development of carcinogen-induced large bowel carcinomas in rats. CD-Fischer rats were given carcinogenic pretreatment with intrarectal instillation of 2 mg of methylnitrosourea 3x a wk from the 1st to the 5th wk, in order to produce large bowel tumors. Thereafter, peroral administration of a high or low dose of indomethacin dissolved in drinking water (20 ug or 10 ug indomethacin/ml tap water) for 15 wk was started at the 11th wk, before the tumors developed. At autopsy in the 26th wk just after the completion of the 15-wk treatment, the incidence of developing large bowel tumors was significantly reduced in treated rats, compared to untreated control rats; 17% or 14% vs 67%. However, at autopsy in the 36th wk, 10 wk after cessation of the treatment, the development of tumors in treated rats was significantly increased. Thus, indomethacin inhibited the development of methylnitrosourea-induced large bowel tumors in rats. The effectiveness of peroral administration of indomethacin was comparable to that of intraperitoneal administration. It is postulated that treatment with this drug may effectively prevent the development of large bowel cancer in patients at high risk. (Author abstract) (23 Refs)

28. ZINC DEFICIENCY, METHYL BENZYL NITROSAMINE CARCINOGENESIS AND DNA SYNTHESIS IN ESOPHAGEAL MUCOSA OF THE RAT (MEETING ABSTRACT).

Schrager T, Newberne PM
Department of Nutrition and Federal Science, M.I.T., Cambridge, MA
Toxicologist; 2(1):105 1982

Zinc deficiency causes hyperplasia and parakeratosis in the esophageal epithelium of many animal species, and increases susceptibility of this tissue to chemical carcinogens. Male Sprague-Dawley rats were given either a control diet (60 ppm) or a diet deficient in Zn (3 ppm). After one month on these diets, some rats received 2.5 mg/kg body weight methyl-benzyl nitrosamine (MBN), twice a week for three weeks. At the end of the dosing period, one group of control ad libitum animals was switched to zinc deficient diet and one group of zinc deficient was switched to control diet. Zinc deficiency throughout the experiment significantly enhanced tumor incidence. Switching diets gave equivocal results. After one month on diets the zinc deficient diet only, led to much greater DNA synthetic activity than the control diet. Following the first dose of MBN, DNA synthetic activity dropped to background levels for both groups but exceeded background at end of dosing. Ten days after the last dose of MBN, DNA synthesis was significantly greater in the control groups. (no Refs)

29. POTASSIUM INHIBITION OF 1,2-DIMETHYLHYDRAZINE-INDUCED COLON CARCINOGENESIS (MEETING ABSTRACT).

Jacobs MM
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Proc Am Assoc Cancer Res; 23:345 1982

A reduction in the 1,2-dimethylhydrazine (DMH)-induced colon tumor incidence by potassium in Sprague Dawley (SD) rats is demonstrated. Male SD rats were injected weekly with 20 mg DMH/kg body weight for 20 weeks. Potassium supplemented drinking water was initiated 1 week before the first DMH treatment and was continued until sacrifice 14 weeks after the last DMH treatment. Rats provided 0.5% K (potassium chloride) in the drinking water and Wayne Lab-blox diet were ingesting 2-fold more potassium than the unsupplemented controls. At sacrifice the incidence of DMH-induced colon tumors was significantly reduced to 70% (12/17) with the potassium additive compared to 100% (13/13) in the DMH controls receiving no supplemental potassium. Potassium also reduced the mean diameter of the tumors and appeared to shift the location of the tumors from the proximal to the transverse and distal colon. The predominant extracolonic tumors induced by DMH were ear duct, pancreatic and small intestine. All were reduced by potassium. Survival was better in potassium plus DMH treated rats (85%) than in the DMH only control (65%). At the level tested potassium did not affect the weight gain of the animals. The reduction in colon tumor incidence may be due to potassium inhibition of DMH activation, enhancement of DMH detoxification or to modification of other cellular processes associated with DMH carcinogenesis. (no Refs)

30. EFFECT OF A MARGINALLY LIPOTROPE-DEFICIENT DIET ON METHYLAZOXYMETHANOL ACETATE CARCINOGENESIS.

Kato K, Mori H, Takahashi M, Hirono I
Dept. Pathology, Gifu Univ. Sch. Medicine, Gifu, Japan
Nutr Cancer; 3(4):234-239 1982

The effect of a lipotrope-deficient diet on methylazoxymethanol acetate (MAM acetate) intestinal carcinogenesis was studied in 2 groups of ACI rats. For 10 wk, weanling rats were fed a semisynthetic diet that was either high in fat and marginally deficient in the lipotropes (Group 1), or adequate for rats in all known respects (Group 2). Four wk after the start of the experimental diets, the animals were given a weekly SC injection of MAM acetate, 25 mg/kg body weight, for a total of 5 times. Following the termination of the experimental diets, the animals were fed a basal diet until the end of the experiment (480 days). The tumor incidence in the jejunum-ileum and the number of tumors in the colon were significantly higher in Group 1 than in Group 2. These results suggest that a marginally lipotrope-deficient diet enhances MAM acetate carcinogenesis, probably in its early stage. (Author abstract) (14 Refs)

31. MODIFICATION OF N-DIETHYLNITROSAMINE-INDUCED CARCINOGENESIS BY CLONIDINE, CAFFEINE, AND ETHANOL.

Gurkalo VK, Zabezhinskii MA
N. N. Petrov Res. Inst. Oncology, Leningrad, USSR
Eksp Onkol; 4(3):25-29 1982

Roles of adrenergic and cholinergic receptors in the mechanism of chemical carcinogenesis were studied in random-bred male rats. The rats received drinking water containing N-diethylnitrosamine (DENA: 70 mg/liter) for 4 mo. Rats in Group 1 received DENA alone those in Group 2 received DENA in combination with clonidine (0.05 mg/kg, ip), those in Group 3 received DENA in combination with ethanol (2 ml/rat, po), and those in Group 4 received DENA in combination with caffeine (3.5 mg/kg, sc). The animals were sacrificed 6 mo after initiation of the experiment, and growths of esophageal and liver tumors that were induced were determined. Histological examination of neoplastic changes in the esophagus and liver showed that caffeine stimulated the DENA-induced carcinogenesis, while clonidine and ethanol inhibited the carcinogenesis. Therapeutic administration of clonidine produced marked inhibition of the DENA-induced liver tumors. Changes in acetylcholinesterase activity in the brain during the DENA carcinogenesis indicated that the modifying effects of clonidine, caffeine, and ethanol were associated with stimulation and inhibition of the autonomic nervous system. (25 Refs) (In RUS)

32. INHIBITION OF 1,2-DIMETHYLHYDRAZINE INDUCED COLON CANCER IN BALB/C MICE BY DEHYDROEPIANDROSTERONE (MEETING ABSTRACT).

Nyce JW, Magee PN, Schwartz AG
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Proc Am Assoc Cancer Res; 23:359 1982

Dehydroepiandrosterone (DHEA) and DHEA-sulfate are major adrenal secretory products in the human with no known biological functions. DHEA is a potent non-competitive inhibitor of mammalian glucose-6-phosphate dehydrogenase, the first enzyme in the pentose-phosphate shunt, a major source of extra-mitochondrial NADPH and ribose-phosphate. Yen et al have reported that long-term treatment of VY-Avy/a mice with DHEA inhibits weight gain without suppressing appetite, possibly by inhibiting lipogenesis as a result of a reduction in pentose-phosphate shunt activity. The well documented observation that reducing weight gain of laboratory rodents by caloric restriction inhibits many types of tumor formation led us to speculate that DHEA might also have an anti-carcinogenic effect. A single ip injection (10 mg/kg) of DHEA inhibited the tetradecanoylyphorbol acetate (TPA)-stimulation of 3H-thymidine incorporation in mouse epidermis, suggesting that the steroid may inhibit tumor promotion. In current studies 153 weanling Balb/c mice were given mouse chow (controls) and 141 mice received mouse chow containing 0.6% DHEA. All mice were injected weekly with 1,2-dimethylhydrazine (21mg/kg,sc). After 26 weeks of treatment, 10 mice were killed in each group. A mean of 13.2 colon tumors were found in the controls and 2.5 in the DHEA treated. In addition, 26/153 control mice and 0/141 DHEA treated had tumors appearing at the anus. (no Refs)

33. PROTECTIVE EFFECTS OF THE HERBICIDE TRIFLURALIN ON BENZO(A)PYRENE INDUCED PULMONARY ADENOCARCINOMA AND FORESTOMACH PAPILLOMAS IN FEMALE A/J MICE (MEETING ABSTRACT).

Triano EA, Lang WR, Kratky MT, Triolo AJ
Departments of Pharmacology and Pathology, Jefferson Medical College of Thomas Jefferson University, Philadelphia, PA, 19107
Fed Proc; 41(3):1548 1982

Mice were fed trifluralin (TF) at 1000, 1500, and 2000 ppm in the diet for 12 or 14 weeks. Tumors were induced by administering 3 mg of benzo(a)pyrene (BP) orally at two time periods. An inhibition of tumorigenesis in lung and forestomach by TF was observed when this herbicide was fed in the diet starting either one week before or one week following exposure to BP. Lung tumors were identified as bronchioloalveolar adenocarcinoma and forestomach tumors as squamous cell papillomas. BP is generally considered to be carcinogenic by virtue of its transformation by microsomal enzymes into chemically reactive intermediates which bind to critical macromolecules of target organs susceptible to tumors. Arylhydrocarbon hydroxylase (BP hydroxylase), a microsomal mixed-function oxygenase, was significantly increased in target (lung and forestomach) and in non-target (glandular stomach) organs when mice were fed TF for a duration of 14 weeks. No significant effects of TF were observed on hepatic enzyme activity. TF was found to decrease the binding of H3-BP to certain liver macromolecules. These findings suggest that various mechanisms resulting from TF treatment may be involved in the observed protection against BP-induced tumors. (no Refs)

34. JEJUNOILEAL BYPASS STIMULATES CELL PROLIFERATION AND ENHANCES EXPERIMENTAL CARCINOGENESIS IN RAT LARGE BOWEL (MEETING ABSTRACT).

Bristol J, Wells M, Williamson R
Department of Surgery, Bristol Royal Infirmary University of Bristol, Bristol BS2 8HW, England
Proc Am Assoc Cancer Res; 23:233 1982

Thousands of small-bowel bypasses have been performed in the management of morbid obesity, but the effects of this procedure on the colon are unknown. We examined the influence of jejunoileal bypass (JIB) on carcionogensis and cell proliferation in the rodent large bowel. Male Sprague-Dawley rats were given either azoxymethane (AOM) 15 mg/kg body weight, or vehicle, by subcutaneous injection weekly for six weeks. One week later, each was subjected to either 85% end-to-side JIB, or sham JIB (jejunal transection, ileotomy, and resuture). At sacrifice 30 weeks postoperatively gut tumors were excised and examined histologically. In vehicle-injected animals colonic length and wet Weight were measured, and the crypt cell production rate (CCPR) was estimated at two sites in the large bowel by counting vincristine-arrested metaphases in individually microdissected crypts. In rats given AOM the median number of large bowel tumors increased from 3 to 8 after JIB. No tumors were found in vehicle-treated animals, but JIB increased colonic length by 19% and wet weight by 29%. CCPR in mid-descending colon was raised from 4.1 +/-0.8 to 13.7 +/-0.8 cells/crypt/hour, and a similar rise occurred in the transverse colon. JIB enhances experimental large bowel carcinogenesis, probably by stimulating colonic crypt cell proliferation. (no Refs)

35. CONVERSION OF METHYL-N-AMYLNITROSAMINE (MNAN) BY RAT ESOPHAGUS TO METABOLITIES BEARING THE N-NITROSO GROUP (MEETING ABSTRACT).

Mirvish SS, Smith JW, Issenberg P
Eppley Institute Research Cancer, University Nebraska Medical Center, Omaha, NE, 68105
Proc Am Assoc Cancer Res; 23:328 1982

A possible explanation for MNAN carcinogenesis in rat esophagus is that this organ converts MNAN into proximal nitrosamine carcinogens. Hence 4 esophagi (slit, 0.51 g) or 1 g liver slices from untreated MRC-Wistar rats were incubated (3 h, 37 degrees) in 20 mL Eagle's medium containing 3 or 30 mg/L of MNAN. The medium was filtered, absorbed on Celite, and eluted with 100 mL methylene chloride. This was concentrated to 1 mL and 5-10 uL analyzed by gas chromatography. MNAN eluted at 4.5 min. With 3 mg/L MNAN, esophageal metabolites eluted at 25 (0.79% yield from MNAN), 29 (0.22%) and 35 min (0.43%); liver metabolites eluted at 19 (0.98%), 29 (0.31%) and 35 min (1.42%, largest fraction). With 30 mg/L MNAN, both tissues produced the 25-min metabolite. Hamster esophagus (insensitive to nitrosamine carcinogenesis) showed little MNAN metabolism at 3 mg/L, but hamster liver behaved like rat liver. Urine (48 h) of rats injected with 30 mg/kg of MNAN, analyzed after beta-glucuronidase treatment, showed metabolites eluting at 19, 21, 29 and 35 min, totaling 0.4% of MNAN dose. Urinary metabolites were destroyed by 366-nm UV irradiation, confirming the N-nitroso function, and behaved as neutral compounds on solvent partition. Hence rat esophagus produced MNAN metabolites that were N-nitroso compounds, one of which was organ-specific at a low MNAN level. (no Refs)

36. EFFECT OF BUTYLATED HYDROXYANISOLE (BHA) ON DOSE-RESPONSE FOR BENZO(A)PYRENE (BP) METABOLITE-DNA ADDUCTS IN MICE (MEETING ABSTRACT).

Anderson MW, White CM, Adriaenssens PI
National Institute of Environmental Health Science, Research Triangle Park, NC, 27709
Proc Am Assoc Cancer Res; 23:355 1982

The phenolic antioxidant, BHA, has been shown to be a potent inhibitor of the neoplastic effects of BP in mouse lung and forestomach. We previously showed that BHA treatment of mice inhibited BP metabolite-DNA adduct formation in the lung to the same degree that BP-induced pulmonary adenoma formation was inhibited. In this study the formation of BP metabolite-DNA adducts in lung, liver, and forestomach of control and BHA-treated female A/HeJ mice was examined as a function of BP dose (po) ranging from 2 to 1350 umol/kg. The major identified adduct in each tissue at each dose was the 7beta,8alpha-dihydroxy-9alpha,10alpha-epoxy-7,8,9,10 tetrahydro-BP (BPDEI)-deoxyguanosine adduct. The 7beta,8alpha-dihydroxy-9beta, 10beta-epoxy-7,8,9,10-tetrahydro-BP (BPDEII)-deoxyguanosine adduct and a BP-phenol-oxide-DNA adduct were also observed. In untreated animals the dose-response curves for these adducts were sigmoidal in each tissue. In forestomach the dose-response curve for BPDE-DNA adducts levels in BHA-treated mice was parallel to the curve for control animals and, thus, the inhibition (45%) of adduct formation was independent of BP dose. In contrast, BHA treatment diminished the curvilinear nature of the dose-response curves for BPDE adducts in lung and live. The dose-response curves in lung and liver of treated animals were approximately linear. The inhibition in lung (70%) and liver (80%) was highest at a BP dose of 0.3 mmol/kg. As BP dose approached zero, the inhibition of BPDE-DNA adduct formation decreased with BP dose and approached values of 40% (lung) and 55% (liver). (1 Ref)

37. A MORPHOLOGIC AND KINETIC BASIS FOR THE MORE INVASIVE CHARACTER OF MNNG-INDUCED DUODENAL TUMORS FOLLOWING PYLOROPLASTY (MEETING ABSTRACT).

Deschner EE, Salmon RJ
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Proc Am Assoc Cancer Res; 23:201 1982

MNNG (N-Methyl-N'-nitro-N-nitrosoguanidine) was delivered in the drinking water (83 mg/l) to 19 male Wistar rats while 8 served as controls. After 12 weeks treatment, a pyloroplasty was carried out on 9 MNNG treated rats and 3 controls. The remaining 10 MNNG-treated rats and 5 controls received no further treatment. Animals given MNNG and sacrificed 26 weeks later had severe dysplasia in the duodenal mucosa while those given MNNG plus a pyloroplasty had massive invasive adenocarcinomas. Pyloroplasty alone or in combination with MNNG decreased the average number of DNA synthesizig cells per column compared with the values from the respective control or MNNG-treated mucosa. In the carcinogen treated duodenal mucosa, individual long crypt columns were seen with 120-132 epithelial cells and 15% greater numbers of 3HTdR (thymidine) labeled cells than in the adjacent mucosa. However, a 3 fold increase in the number of these hyperactive columns was found in the MNNG plus pyloroplasty group. Moreover in the latter group, 26.5% of the columns were longer (133-238 cells) and contained almost double the number of labeled cells/column seen in the surrounding mucosa (18.1 vs 9.4). The increased severity of the tumors in the pyloroplasty group appears to be related to the greater incidence and enhanced proliferative nature of the hyperactive columns. (1 Ref)

38. GASTRIN PROTECTION AGAINST CHEMICALLY INDUCED GASTRIC ADENOCARCINOMAS IN WISTAR RATS: HISTOPATHOLOGY OF THE GLANDULAR STOMACH AND INCIDENCE OF GASTRIC ADENOCARCINOMA.

Tatsuta M, Yamamura H, Taniguchi H, Tamura H
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JNCI; 69(1):59-66 1982

The effects of gastrin on the histopathology of the glandular stomach and on the incidence of gastric carcinoma induced by N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) were investigated in inbred Wistar (W) rats. Prolonged administration of gastrin after treatment with MNNG significantly reduced the incidence of adenocarcinomas of the glandular stomach. In addition, atypical glandular proliferations were significantly less frequent and were smaller, and the incidence of marked mucosal atrophy was significantly reduced in both the antral and oxyntic gland mucosae. Both atypical glandular hyperplasia and mucosal atrophy are precursors of gastric cancers; prolonged administration of gastrin to rats after treatment with MNNG suppressed development of precursors of gastric cancer and so prevented development of gastric cancers. (Author abstract) (19 Refs)

39. EFFECT OF SEX HORMONES ON THE EXPERIMENTAL INDUCTION OF CANCER IN RAT STOMACH - A PRELIMINARY STUDY.

Furukawa H, Iwanaga T, Koyama H, Taniguchi H
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Digestion; 23(3):151-155 1982

The effects of sex hormones on the induction of gastric carcinoma by N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) were investigated in Wistar rats. Well-differentiated adenocarcinomas developed with high frequency (88%) on the glandular stomach of male rats given MNNG in drinking water (50 ug/ml) for 4 mo and sacrificed on the 12th mo of the experiment. In female rats given MNNG, no gastric cancer was observed. In the castrated or estradiol-treated male rats, the incidence of carcinoma was lower (29 and 68%, respectively) than in the nontreated male rats. Histologically, poorly differentiated adenocarcinomas were observed more frequently in these groups than in the nontreated male group. In MNNG carcinogenesis, female, castrated male and estrogen-treated male rats had a lower incidence of gastric cancer with lower histological differentiation than did nontreated male rats. (Author abstract) (11 Refs)

40. ORNITHINE DECARBOXYLASE INDUCTION IN RAT COLON: SYNERGISTIC EFFECTS OF INTRARECTAL INSTILLATION OF SODIUM DEOXYCHOLATE AND STARVATION-REFEEDING (MEETING ABSTRACT).

Stanley BA, Kazarinoff MN
Cornell University, Ithaca, NY, 14853
Fed Proc; 41(3):355 1982

Starvation-refeeding, intrarectal instillation of the known colon tumor promoter sodium deoxycholate (NaDC), and a combination of starvation-refeeding with NaDC instillation were compared for their effects on ornithine decarboxylase (ODC) activity in the colon of male Sprague-Dawley rats. Starvation (48h) and refeeding (12h) led to a 5-fold increase in ODC levels compared to ad lib fed controls, while NaDC

(24mM) led to a 3-fold rise in ODC levels 4.5 after instillation. The combination of the two treatments gave a synergistic 16-fold increase over controls. Complicating effects of immediate food consumption were avoided by removing food 6h before sacrifice of all groups. Starvation-refeeding also induced rat liver ODC, but synergism with thioacetamide or dexamethasone, known inducers of liver ODC, was not seen. The synergism observed in colon may indicate that the treatments act via different mechanisms to induce ODC. Our working hypothesis is that the increased ODC level seen after starvation-refeeding reflects an increase in general macromolecular synthesis, while the increased ODC level seen after NaDC instillation reflects a specific increase in ODC synthesis. The synergistic enhancement of tumor promoter-related ODC induction by a dietary pattern (rather than a dietary component) suggests a new area for investigation of potential nutrition-cancer interactions. (no Refs)

41. INHIBITION OF BIS(2-OXOPROPYL)NITROSAMINE-INDUCED COLON CARCINOGENESIS IN THE RAT DIETARY SELENIUM (MEETING ABSTRACT).

Birt DF, Runice CE, Julius AD, Salmasi S, Ryan W
University of Nebraska Medical Center, Omaha, NE, 68105
Proc Am Assoc Cancer Res; 23:349 1982

Dietary selenium (Se) was fed at levels of 0.1 and 2.0 ppm to MRC rats from 7 weeks of age until termination of the study at 58 weeks of age. Weekly injections of bis-(2-oxopropyl)nitrosamine (BOP) (5 mg/kg body weight, sc) began at 8 weeks of age and continued for the duration of the study. Body weights were not influenced by BOP treatment in either sex, or by Se treatment in males. However female body weights were decreased by feeding 2.0 ppm Se by comparison with 0.1 ppm Se for 50 weeks. Determinations of whole blood Se, and plasma and erythrocyte glutathione peroxidase activity (GSH-Px)- were made at 0, 10, 25 and 50 weeks after BOP treatment began. Blood Se rose with dietary Se at all intervals and plasma GSH-Px rose with dietary Se at 25 and 50 weeks, but neither measurement was influenced by carcinogen treatment. In addition erythrocyte GSH-Px increased with dietary Se at 50 weeks and was decreased after 25 weeks of BOP treatment at the low Se levels. The yield of colon adenocarcinomas was reduced in male rats from 32 in 26 rats in the 0.1 ppm Se group to 17 in 29 rats in the 2.0 ppm Se group. Adenocarcinoma incidences dropped from 50% to 28% in these groups. Colon adenocarcinomas were not induced in rats not treated with BOP or in female rats fed either selenium level and treated with BOP. (no Refs)

42. INDUCTION OF COLON MUCOSAL B-GLUCURONIDASE PRODUCTION AS A MECHANISM FOR 1,2-DIMETHYL-HYDRAZINE COLON SPECIFICITY (MEETING ABSTRACT).

Celik C, Lewis DA, Paloini NS, Holyoke ED
Roswell Park Memorial Institute, Buffalo, NY, 14263
Proc Am Assoc Cancer Res; 23:324 1982

Although early studies in germ free rats showed almost complete dependence of dimethylhydrazine (DMH) colon carcinogenesis upon the presence of colon bacteria, no adequate explanation was given for the 20% tumor incidence observed in germ free animals. Bacterial activation of liver microsomal products releasing active proximate carcinogens has been the accepted reason for the exquisite specificity DMH has for the colon. Recent work, including the present study, show the colon mucosa is capable of metabolizing carcinogens and activating conjugated forms metabolized in the liver independent of the intestinal microflora. Mucosal B-glucuronidase production was assayed in coded, scraped mucosa samples from the duodenum/jejunum, ileum, right colon, and left colon of normal and DMH treated rats. Normal mucosal B-glucuronidase production was highest in the left colon followed by the right colon, duodenum, and ileum respectively. Enzyme production in the left colon was significantly increased 24 hours after injection of 25mg/kg body weight DMH. No elevation was seen in other mucosal samples. Metabolism of DMH to oxidated forms conjugated to glucuronic acid is well established. Thus, this study offers a possible role for carcinogen induction of a metabolic enzyme in its target tissue. (no Refs)

43. EFFECT OF DIETARY FAT AND ANTIOXIDANT ON INCIDENCE OF SPONTANEOUS AND 1,2-DIMETHYLHYDRAZINE-INDUCED TUMORS IN MICE (MEETING ABSTRACT).

Brown RR, Erturk E, Arend RA, Potera C, Remus N, Ruzicka E, Dallmann L
University of Wisconsin Center for Health Sciences, Madison, WI, 53792
Proc Am Assoc Cancer Res; 23:277 1982

In attempts to further define the role of type and quantity of dietary fat and antioxidants on cancer incidence, we studied tumor incidence (spontaneous and dimethylhydrazine (DMH) induced) in mice fed semipurified diets having one of 5 different vegetable fat mixes containing respectively 59% saturated (SAT), 60% monoene (MUF), 59% diene (DUF), 35% trans-monoene (TRN), or 4% triene (TUF). Butylatedhydroxyanisole (BHA) was added to some SAT and TUF diets. Weanling CD-1 mice of both sexes (40/group) and female C3H (60/group) were fed these diets having 5% or 17% fat substituted isocalorically for sucrose. Treated mice received 10 weekly subcutaneous injections of 0.25 mg DMH freshly neutralized. Controls received buffer only. DMH caused liver tumors and a few kidney and lung tumors and splenic leukemia, but no colon tumors. More DMH-induced liver and lung tumors were seen in males fed 5% TRN than in other groups but this was not confirmed in males fed 17% TRN. Total tumors in males fed 17% and 5% fats were not different suggesting that when fed isocalorically, the quantity of fat did not influence tumor incidence in CD-1 males. BHA reduced the DMH-liver tumor rate in 17% SAT but not in 17% TUF. DMH-liver tumors were fewer in 17% SAT than in 17% TUF males and this difference was even greater between SAT+BHA+DMH and TUF+BHA+DMH groups. (no Refs)

44. EFFECT OF DIET ON THE METABOLISM OF 1,2-DIMETHYLHYDRAZINE (DMH) IN THE RAT (MEETING ABSTRACT).

Glauert HP, Bennink MR
Michigan State University, East Lansing, MI, 48824
Fed Proc; 41(3):356 1982

Dietary fat and liver have been shown to influence DMH-induced colon carcinogenesis in experimental animals. One possible mechanism is that diet alters DMH metabolism. In this experiment, we examined the effect of dietary fat, wheat bran, and agar on 1) the metabolism of DMH to products which bind to DNA in rat colon epithelial cells (CEC), and 2) the clearance of DMH and its metabolites from blood. Diets were fed for four weeks; labeled DMH was then injected ip and rats were killed at various time intervals (12-96 hours). CEC were isolated from the colon and DNA was purified from CEC.

Maximum binding DMH metabolites to DNA was seen 36 hours after the injection of DMH. The amount of 14C binding to DNA was not altered by diet but a diurnal variation was evident. Maximum 14C binding at 9 pm was 32-109% greater than 14C binding at 9 am. Serum radioactivity was greater in rats fed the high-fat diet and lower in rats fed the wheat bran compared to the control group. 14C disappearance from serum fit a 'two-pool model' with half-life for the first pool ranging from 27 to 33 hr and half-life for the first pool ranging from 62 to 71 hr; diet did not alter half-life for either pool. This experiment shows that diet does not alter the amount of DMH metabolites bound to DNA in CEC even though diet does change the level of DMH plus its metabolites in serum. It appears that there is a marked diurnal variation in DMH metabolism. (no Refs)

45. IMMUNE REACTIONS IN INADEQUATE NUTRITION AND IN AFLATOXIN CARCINOGENESIS.

Popov AA, Krystev LP, Kamenova BB
Inst. Gastroenterology and Nutrition, Sofia, Bulgaria
Vopr Pitan; (3):58-60 1982

Relationships between inadequate nutrition, humoral immunity, and incidence of aflatoxin-induced tumors were studied in male Wistar rats. The aflatoxin was administered ip, 10 ug/rat, 5x/wk. Rats in Group 1 received standard nutrition, while rats in Group 2 received a reduced ration. Colonic leiomyosarcomas, but no hepatomas, were observed to develop. The incidence of the sarcomas in the Group 2 rats was significantly lower than that in the Group 1 rats. The reduced incidence of aflatoxin-induced tumors in the Group 2 rats was shown to be associated with immunological deficiency. It was assumed that the immune deficiency was accompanied by inhibition of enhancement in the course of aflatoxin carcinogenesis. (14 Refs) (In RUS)

BIOCHEMICAL, MORPHOLOGICAL AND IMMUNOLOGICAL ASPECTS OF GI CARCINOGENESIS

46. CARCINOGEN-INDUCED DNA DAMAGE AND CELLULAR ALTERATIONS IN F344 RAT COLON ORGAN CULTURES.

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JNCI; 68(6):1015-1022 1982

Optimized culture conditions were used to achieve prolonged survival of colon mucosa from conventional inbred F344 strain rats. Up to 21 days in culture, a high percentage of explants had viable mucosa with intact crypt columns and maintained active replicative DNA synthesis in the proliferative zone of the crypts. An acute 4-hr in vitro exposure to 0.5 mM of the colon-selective carcinogens 1,2-dimethylhydrazine dihydrochloride (DMH) and N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) produced 26 and 78% suppressions of replicative DNA synthesis, respectively, whereas the same exposure to the liver carcinogen dimethylnitrosamine produced only a 5% suppression. the thymidine-labeling index of DMH-exposed cells was lower than that of control cells at 1 day and then increased above the control values 7-21 days later. MNNG exposure produced pronounced morphologic changes in the crypt columns. MNNG-exposed cultures that were transplanted into the mammary fat pads of syngeneic female rats produced hypercellular cysts different from those formed by nonexposed fragments. These findings indicate that the acute and persistent effects of colon carcinogens can be studied directly on the target tissue in organ cultures. (Author abstract) (46 Refs)

47. CHANGES IN THE CYCLIC NUCLEOTIDE SYSTEM IN 1,2-DIMETHYLHYDRAZINE INDUCED RAT INTESTINAL ADENOCARCINOMAS.

Loven DP
The University of Iowa, Iowa City, IA
Diss Abstr Int [B]; 42(7) 1982

The cAMP (cyclic AMP) content of the adenocarcinoma was lower than either normal intact intestine or the mucosal layer. The cAMP content of intact intestine distant from any visible lesion in tumor bearing animals was similar to normal intact intestine. The cAMP content of intact intestine adjacent to the adenocarcinoma was similar to the tumor. The (cyclic guanosine monophosphate) cGMP content of the adenocarcinoma was elevated compared to the normal intact intestine, but was unchanged compared to the normal intestinal mucosa. The cGMP content of intact intestine distant from any visible lesions in tumor bearing animals was similar to the normal intact intestine. The cGMP content of intact intestine adjacent to the adenocarcinoma was similar to the tumor. Isoproterenol, carbachol, and PGE2 (prostaglandin E2) caused a greater increase in cAMP in normal colon mucosa compared to the colon adenocarcinoma in vitro. The basal and total adenylate cyclase activity was depressed in broken tumor cell preparations compared to normal colon mucosa. Agents added in vitro similarly affected the cGMP content of colon adenocarcinoma and normal colon mucosa. The basal guanylate cyclase activity of broken cell preparations of colon adenocarcinoma and normal colon mucosa were similar, however, the total guanylate cyclase activity was depressed in the tumor compared to normal colon mucosa. The cAMP phosphodiesterase activity of the colon adenocarcinoma was elevated compared to normal colon muscosa. The cGMP phosphodiesterase activity of the colon tumor was similar to normal colon mucosa. The cAMP dependent protein kinase activity of the colon adenocarcinoma was depressed compared to normal colon mucosa. (no Refs)

48. COMPARISON OF METABOLISM OF BENZO(A)PYRENE (BP) BY HAMSTER AND RAT KIDNEY, LIVER, INTESTINE, LUNG AND TRACHEA CELLS IN CULTURE (MEETING ABSTRACT).

Rainer R, Hillesund T, Ernst MK, Polley JA
Litton Bionetics, Inc., Kensington, MD, 20895
Proc Am Assoc Cancer Res; 23:329 1982

The metabolism of BP was compared using reverse phase HPLC (high pressure liquid chromatography) and by determination of levels of covalent binding, with cultured kidney, liver, small intestine, lung and trachea from male Syrian golden hamsters and Sprague-Dawley rats. Hepatocytes from both species metabolized BP to a 3 to 5 times greater extent than the other cells studied. Formation of water-soluble metabolites by hepatocytes was at least 10 times that of the other cells, accounting for their greater activity. Generally hamster cells had greater metabolic capability than rat cells. High levels of BP-9,10-dihydrodiol and BP-7,8-dihydrodiol (12 pmoles/ml medium) were observed with hamster hepatocytes as well as with rat hepatocytes, kidney, intestine and lung cells. Levels of covalent binding of metabolites of BP were at least 10 times greater in hepatocytes from both species than in the other cell types. Binding to hepatocytes and hamster embryo cells increased with incubation time coinciding with an increase in the formation of water-soluble and diol metabolites. The metabolic potential of intact cell systems was assessed by determination of the formation of organic-soluble and conjugated metabolites, as well as of the activation of BP through covalent binding. These studies suggest the potential usefulness of these cells for metabolic activation in vitro test systems. (no Refs)

49. ESOPHAGEAL AND HEPATIC MICROSOMAL METABOLISM OF N-NITROSO-METHYLBENZYLAMINE (NMBZA) AND N-NITROSODIMETHYLAMINE (NDMA) IN THE RAT (MEETING ABSTRACT).

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Ontario Cancer Institute, Toronto, Ontario, M4X 1K9, Canada
Proc Am Assoc Cancer Res; 23:311 1982

The metabolism of the rat esophageal carcinogen, NMBzA, and the rat hepatocarcinogen, NDMA, was compared using microsomes prepared from the respective target and non-target tissues. Each compound (5mM) was incubated with microsomes and an NADPH generating system. Hepatic microsomes metabolized NDMA to formaldehyde (dimedone assay), and NMBzA to formaldehyde, benzaldehyde and benzyl alcohol (high performance liquid chromatography assay). The overall rates of metabolism of the nitrosamines were similar. However, hepatic microsomal metabolism of NMBzA at the methylene carbon proceeded at 10 times the rate of metabolism at the methyl carbon. In contrast, microsomes from esophageal mucosa metabolized NMBzA to benzaldelyde and formaldehyde only; benzyl alcohol formation was not detected. The rate of benzaldehyde formation was 100 times that of formaldehyde. The esophageal metabolizing system was exclusively located in the mucosa, and preferentially in the microsomal subcellular fraction. The system exhibited properties typical of a cytochrome P-450 pathway, being NADPH dependent, and being inhibited by CO and SKF 525-A, but was unaltered by either phenobarbitone or 3-methylcholanthrene pretreatment. The results indicate that hepatic microsomes metabolize both compounds to a similar extent. In contrast, esophageal microsomes preferentially metabolize the esophageal carcinogen, NMBzA, and the metabolizing system may thus play a role in determining which chemicals induce tumors in the rat esophagus. (no Refs)

50. ALTERATION OF TISSUE LEVELS AND METABOLISM OF BENZO(A)PYRENE BY ANTI-BENZO(A)PYRENE ANTIBODIES (MEETING ABSTRACT).

Kantrowitz JD, Flynn EJ
Department of Pharmacology, New Jersey Medical School, Newark, NJ, 07013
Fed Proc; 41(3):1549 1982

The disposition of benzo(a)pyrene (BP) in mice can be altered by the administration of anti-BP antibodies. Assay of various tissues from mice which had received 3H-BP intravenously showed that the tissue:plasma ratio for BP was less in immunized mice than in controls. Initial plasma concentrations in immunized mice were seven times higher than controls following intravenous injection of H3-BP. In addition, the rate of decay (beta phase) was much faster in the immunized group. Further inspection revealed a greater percentage of the plasma BP was protein bound in the immunized group as compared to controls. The difference in the rate of decay was primarily due to the bound form of BP (half-life of 10.4 hrs for immunized vs 20.1 hrs for control), since the difference in the half-lives of the free BP differed little (23.2 hrs vs 27.4 hrs). This greater rate of decay of BP in immunized mice was paralleled by an increase in radioactivity excreted into the gastrointestinal tract. Analysis of ethyl acetate-extractable metabolites from the GI (gastrointestinal) contents by HPLC (high pressure liquid chromatography) revealed that less parent BP was being broken down to metabolites in immunized mice than in controls. (no Refs)

51. FUNCTIONAL SIGNIFICANCE OF THE INTESTINAL IMMUNE SYSTEM. AN OVERVIEW. PART 2: PATHOLOGY.

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Pathologisches Institut, Universitat Hamburg, Martinistr. 52, D-2000 Hamburg 20, W. Germany
Z Gastroenterol; 20(5):245-256 1982

Immunopathogenic mechanisms of various intestinal diseases are reviewed. Immuno-inflammatory diseases such as ulcerative colitis and Crohn's disease, immuno-proliferative diseases such as alpha-chain disease and malignant lymphoma, and immunodeficiencies are presented. Defects in the intestinal immune system may produce local or systemic effects. Chronic inflammatory conditions produce overstimulation of the IgA-producing cells. Collapse of the IgA defense results in overstimulation of IgG production. IgG may be found in the serum and in the extracellular stroma of the intestinal mucosa. IgG forms local fixed immune complexes. Crohn's disease is characterized by an increase in all classes of immunoglobulin with a predominance of IgA; a sharp increase in IgG occurs in advanced stages of the disease, at which time a transmural inflammation is found. The etiology and pathogenesis of chronic inflammatory diseases is uncertain. Immuno-proliferative diseases are often associated with parasitic infestation. Overstimulation of the immune system by the parasites leads to malignant transformation. Malignant lymphomas include various types and can be classified as those developing from a prior inflammatory condition and those developing without prior disease. Immunodeficiencies may involve the lack of immune capacity or the development of immune tolerance. Immunodeficiencies increased the susceptibility to malignant transformation. (102 Refs) (In GER)

52. SEQUENTIAL MORPHOLOGICAL STUDIES OF THE ESOPHAGEAL CARCINOMA OF RATS INDUCED BY N-METHLY-N-AMYLNITROSAMINE.

Sasajima K, Taniguchi Y, Okazaki S, Morino K, Takubo K, Yamashita K, Shirota A
First Dept. Surgery, Nippon Medical Sch., Sendagi 1-1-5, Bunkyo-ku, Tokyo, Japan
Eur J Cancer Clin Oncol; 18(6):559-564 1982

N-Methyl-N-amylnitrosamine was given to male Wistar rats in the drinking water at a concentration of 0.003% for 8 weeks. Three rats were autopsied weekly from the 1st to the 25th week. The stages of hyperplasia, dysplasia and squamous cell carcinoma in the esophagus were chronologically observed. Hyperplasia and dysplasia were found by the 6th week and continuously observed until the end of the experiment. Early squamous cell carcinomas were found in the 13th week. They showed endophytic or exophytic growths. Histologically, the endophytic growths were well-differentiated squamous cell carcinomas and the exophytic growths were poorly-differentiated. Advanced carcinomas were first found in the 15th week and were almost well-differentiated. Carcinomas were not found in papillomas. The incidence of carcinomas increased with time, being 9 out of 15 rats (60%) in the final 21st though

25th weeks. Lymph node metastasis was found in one rat, killed at the 24th week. (Author abstract) (9 Refs)

53. ANOMALOUS EXPRESSION OF HLA-DR ANTIGENS ON HUMAN COLORECTAL CANCER CELLS.

Daar AS, Fuggle SV, Ting A, Fabre JW

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J Immunol; 129(2):447-449 1982

Expression of HLA-DR and HLA-ABC antigens was examined in 15 colorectal cancer specimens. All samples of normal colon and rectum were taken from surgical resection specimens from areas distant from the tumors. Two patterns of HLA-DR positivity were observed in the tumor specimens. One pattern exhibited isolated positive cells with malignant cells clearly not staining. In the second pattern an apparently relatively well-differentiated crypt but with intensely HLA-DR-positive epithelium was observed in the longitudinal section. It could not be established whether the observed pattern represented malignant cells attempting to differentiate into normal but HLA-DR-positive epithelial crypts or the induction of HLA-DR antigens in a normal crypt in close contact with the tumor. Of the 15 tumors examined, 8 had patches of HLA-DR-positive malignant cells as observed in the first pattern. No correlation could be seen with degree of differentiation of the tumor, its site of origin, or degree of leukocytic infiltration. Fourteen of the 15 tumors were positive throughout for HLA-ABC antigens. In a very poorly differentiated adenocarcinoma, the staining was obviously weaker, and approx one-half of the tumor mass did no stain at all. The findings might define a biologically important heterogeneity among populations of tumor cells. (17 Refs)

54. HYDROXYLATION AND ACTIVATION OF CARCINOGENS BY HUMAN COLON AND HUMAN COLON TUMOR CELLS (MEETING ABSTRACT).

Newaz SN, Fang WF, Strobel HW

The University of Texas Medical School, Houston, TX, 77025

Fed Proc; 41(3):1564 1982

Microsomes prepared from human colons obtained at autopsy catalyze the hydroxylation of benzo[a]pyrene (BAP) and 1,2-dimethylhydrazine (DMH). The metabolism of DMH was highest in microsomes prepared from the descending colon, intermediate in the transverse colon and lowest in the ascending colon. The metabolism of BAP does not show such an anatomical distribution. Human colon tumor cell line LS174T microsomes also catalyze the hydroxylation of DMH and BAP in an inducible manner. Phenobarbital/hydrocortisone (P/H) induces DMH hydroxylation 3-fold and BAP hydroxylation 10-fold. Benzanthracene (BA) induces BAP hydroxylation 30-fold indicating that these cells have a mixed function oxidase system. Cyclophosphamide (CP) is also hydroxylated to its cytotoxic metabolite by the colon tumor cells as judged by a 33% decrease in cell number. BA induces cyclophosphamide activation and cell killing by 80%, while P/H effects a 76% decrease in cell number as compared with controls. These results show that human colon and human colon tumor cells are totipotent for activation of carcinogens and the antitumor agent cyclophosphamide. (no Refs)

55. DIFFERENCES IN METABOLISM OF CHEMICAL CARCINOGENS IN CULTURED HUMAN EPITHELIAL TISSUES AND CELLS.

Harris CC, Trump BF, Grafstrom R, Autrup H

Lab. Human Carcinogenesis, NCI, NIH, Bethesda, MD, 20205

J Cell Biochem; 18(3):285-294 1982

Activation and deactivation of chemical procarcinogens were studied in cultured, nontumorous human epithelial tissues and cells. Procarcinogens were selected primarily on the basis that they represented several chemical classes and were found in the diet, drinking water, polluted air, and/or tobacco smoke. Conversion of the procarcinogens by cultured human tissues into metabolite(s) that bind covalently to DNA was investigated. Cultured human bronchus converted every procarcinogen studied into forms that bind to DNA. Carcinogens, such as aflatoxin B1, were activated to carcinogen-DNA adducts by cultured human tissues, bronchus, esophagus, colon, and bladder, even though epidemiological studies have not implicated aflatoxin B1 as a cause of cancer at these tissues. Metabolism of benzo[a]pyrene (BAP) and formation of DNA adducts were studied in cultured human tissues collected at the time of immediate autopsy. BAP metabolism and DNA binding were highest in the bronchus. Results indicated that quantitative extrapolations of carcinogen binding data may be possible among some, but not all tissues, and when different chemical classes of carcinogens are compared, quantitative and predictive correlations may frequently not be observed. Differences in carcinogen metabolism among people may be qualitative and/or quantitative. The magnitude of the differences ranges from 50-to 150-fold and is similar to that found in pharmacogenetic studies of drug metabolism. The rate-limiting enzymatic reaction could differ among humans and tissue types. (60 Refs)

56. EFFECTS OF CYCLOPHOSPHAMIDE AND POLYCYCLIC AROMATIC HYDROCARBONS ON CELL GROWTH AND MIXED-FUNCTION OXIDASE ACTIVITY IN A HUMAN COLON TUMOR CELL LINE.

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Cancer Res; 42(9):3676-3681 1982

Human Colon tumor cells (cell line LS174T) retain a cytochrome P-450-containing drug metabolism system capable of hydroxylating polycyclic hydrocarbons and the anticancer drug cyclophosphamide. The hydroxylation of benzo(a)pyrene by human colon tumor cells is highly inducible. Phenobarbital plus hydrocortisone induce benzo(a)pyrene hydroxylation activities 10-fold, while benz(a)anthracene induces the rate of hydroxylation 30-fold. Cytochrome P-450 specific content is increased two- to three-fold by treatment with phenobarbital plus hydrocortisone and benz(a)anthracene, respectively. Addition of cyclophosphamide alone results in no increase in hydroxylation activities but causes a decrease in cell growth rate. The combination of cyclophosphamide with either of the inducers phenobarbital plus hydrocortisone or benz(a)anthracene results in markedly enhanced inhibition of cell growth as judged both by a decrease in the number of cells per plate and in the incorporation of [3H]thymidine into DNA. Thus, these data show that cyclophosphamide is cytotoxic to human colon tumor cells and that the cytotoxicity is enhanced by simultaneous administration of benzo(a)anthracene or phenobarbital plus hydrocortisone to the tissue cultures. (Author abstract) (36 Refs)

57. METABOLIC ACTIVATION OF AFLATOXIN B1 AND BENZO(A)PYRENE IN EXPLANT CULTURES OF HUMAN TISSUE (MEETING ABSTRACT).

Grafstrom RC, Autrup H, Trump BF, Harris CC
National Cancer Institute, Bethesda, MD, 20205
Fed Proc; 41(3):330 1982

Binding of aflatoxin B1 (AFB) and benzo(a)pyrene (BP) to DNA was compared in non-tumorous human bronchial (HB), esophageal (HE), colonic (HC), and duodenal (HD) tissues obtained at the time of either surgery or autopsy. Tissues were incubated for 24 hr with radiolabelled AFB or BP at 1.5 M in a chemically defined medium. The binding level of the carcinogens to epithelial DNA varied widely among tissues and individuals. Binding levels of AFB (pmol carcinogen bound to 10 mg DNA) were as follows: HB (mean 16, range 0-92, cases 28); HE (11, 0-35, 11); HC (8, 0-44, 27); and HD (23, 0-46, 11). Binding levels of BP were: HB (25, 0-160, 26); HE (27, 0-104, 11); HC (8, 0-44, 24); and HD (21, 0-58, 10). Thus, the order of mean binding values among the tissues was for AFB: HD greater than HB greater than HE greater than HC, and for BP: HE greater than HB greater than HD greater than HC. In tissues where the metabolism of both carcinogens was studied, binding of BP was generally higher than that of AFB. Analysis revealed no correlation between binding levels of the two carcinogens in any of the tissue types. The results indicate quantitative differences in carcinogen activation among tissues and demonstrate the variation in carcinogen metabolism among individuals. (no Refs)

58. GROWTH RESPONSES OF RAT STOMACH CANCER CELLS TO GASTRO-ENTERO-PANCREATIC HORMONES.

Kobori O, Vuillot MT, Martin F
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Int J Cancer; 30(1):65-67 1982

Various hormones and peptides were added to rat stomach cancer cells growing in vitro in a serum-free medium and the cell number was determined by a spectro-photometric method. Five gastro-entero-pancreatic hormones or related peptides (tetragastrin, glucagon, secretin, cholecystokinin-pancreozymin and cerulein) significantly increased the number of stomach cancer cells from 150% to 310% of the number of control cells cultivated in a serum-free, hormone-free medium. On the other hand, insulin and vasoactive intestinal peptide, and other hormones (thyroxin, epinephrine, hydrocortisone, beta-estradiol, progesterone, testosterone), peptone broth and bovine serum albumin had no significant growth effect. All the active substances belong to the two major families of gastro-entero-pancreatic polypeptide hormones, suggesting the existence of hormone receptors at the surface of stomach cancer cells. (Author abstract) (10 Refs)

59. INFLUENCE OF GROWTH FACTORS ON PROLIFERATION OF NORMAL AND CHEMICALLY TRANSFORMED RAT ESOPHAGEAL EPITHELIAL CELLS (MEETING ABSTRACT).

Stoner GD, Babcock MS
Department of Pathology, Medical College of Ohio, Toledo, OH, 43699
Proc Am Assoc Cancer Res; 23:162 1982

The proliferative response of normal (N) and N-nitrosomethylbenzylamine-transformed (T) rat esophageal epithelial cells to various growth factors was compared. We have so far determined the effects of several concentrations of dialyzed fetal bovine serum, epidermal growth factor (EGF), 12-O-tetradecanoylphorbol-13-acetate (TPA) and Ca++ on the clonal growth of N and T cells. The cells were seeded into 60 mm dishes and, after 5-7 days, the colonies were fixed, stained and the number cells per colony counted. Growth responses of N and T cells were compared by determining the number of population doublings per day per concentration of growth factor. For optimum clonal growth, N cells required four times as much serum as T cells. Moreover, N cells required serum for clonal growth whereas T cells grew in serum-free medium. EGF did not stimulate the growth of either N or T cells. The growth of T cells was not influenced by TPA whereas that of N cells was inhibited by as little as 0.3 ug/ml. Both N and T cells required a minimum of 10(-5) M Ca++ for clonal growth and reached optimum growth at 10(-4) M. N cells were stimulated to differentiate into keratinizing epithelial cells in medium containing 10(-3) M Ca++ and T cells were not. These data suggest that the difference in serum requirement for clonal growth of N and T cells is due to factors other than EFG and Ca++. (no Refs)

60. HIGH-DENSITY LIPOPROTEINS AND THE PROLIFERATION OF HUMAN TUMOR CELLS MAINTAINED ON EXTRACELLULAR MATRIX-COATED DISHES AND EXPOSED TO DEFINED MEDIUM.

Gospodarowicz D, Lui GM, Gonzalez R

Cancer Res. Inst., Univ. California Medical Center, San Francisco, CA, 94143

Cancer Res; 42(9):3704-3713 1982

The ability of high-density lipoprotein (HDL) to support the growth of an established tumor cell line exposed to defined medium supplemented with transferrin has been examined. Low-density A-431 carcinoma cells maintained on extracellular matrix- or fibronectin-coated dishes proliferated actively when exposed to a synthetic medium supplemented with HDL, 500 ug protein per ml. Epidermal growth factor added at concentrations above 0.5 ng/ml inhibited cell growth, while at concentrations above 5 ng/ml it was cytotoxic. Among the various substrata tested for their ability to support the active proliferation of low-density A-431 cells when exposed to transferrin and HDL, plastic was the least efficient. On fibronectin-coated dishes, cells ceased to proliferate after 8 population doublings, while on extracellular matrix-coated dishes cells could be passaged for 50 population doublings. In the case of colon carcinoma, rhabdomyosarcoma, and Ewing's sarcoma cells exposed to medium supplemented with transferrin, the addition to the cultures of HDL alone resulted in a growth rate and final cell density which were similar to those observed when cells were exposed to serum-supplemented medium. In the case of the mammary carcinoma cell lines MCF-7 and ZR-75-1, HDL also supported cell growth, although to a lesser extent than did serum. The present study therefore indicates that HDL is capable of supporting, either totally or partially, the in vitro proliferation of tumor cells. (Author abstract) (39 Refs)

61. CHARACTERISTICS OF SEVEN CLONES OF THE WIDR HUMAN COLON ADENOCARCINOMA CELL LINE.

Petricciani JC, Smith P, Earley EM, Levenbook I, Noguchi P
Bureau Biologics, Food and Drug Admin., 8800 Rockville Pike, Bethesda, MD, 20205
In Vitro; 18(5):492-494 1982

Seven clonal populations were derived from the WiDr human colon adenocarcinoma cell line and were characterized with respect to chromosome number, DNA content, and tumorigenicity in nude mice. There was no correlation between tumor vol and either DNA content or chromosome number; but there were wide differences among the clones regarding the size of tumors they were able to produce in nude mice. (author abstract) (8 Refs)

PANCREATIC CARCINOGENESIS

62. DEVELOPMENT OF A TRANSPLANTABLE MODEL OF PANCREATIC DUCT ADENOCARCINOMA.

Townsend CM, Franklin RB, Gelder FB, Glass E, Thompson JC
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Surgery; 92(1):72-78 1982

We report here the first development of a continuous cell line in tissue culture of an animal pancreatic duct adenocarcinoma that is histologically similar to human pancreatic duct adenocarcinoma. A primary pancreatic duct adenocarcinoma, induced in a male Syrian golden hamster after 23 wk of weekly sc injections of N-nitrobis(2-hydroxypropyl)amine, was minced and injected sc into three hamsters. After 8 wk, a single tumor was apparent. Subsequent passages of fragments into the cheek pouches were performed at 3-to 4-wk intervals. After five passages, minced fragments of a tumor were placed in tissue culture. Colonies appeared by 7 days; an epithelioid cell line, without fibroblasts, was established by 60 days. Single-cell suspensions, injected into hamster cheek pouches or sc, produced tumors in a dose-dependent fashion. Spent culture medium of tissue culture cells and saline extracts of freshly excised tumors contained pancreatic oncofetal antigen-like activity. (Author abstract) (15 Refs)

63. AUTORADIOGRAPHY AND PATHOLOGY STUDIES OF CIS-2,6-DIMETHYLNITROSOMORPHOLINE IN SYRIAN HAMSTERS (MEETING ABSTRACT).

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National Cancer Institute-Frederick Cancer Research Facility, Frederick, MD, 21701
Proc Am Assoc Cancer Res; 23:197 1982

DMNM, 2,6-Dimethylnitrosomorpholine, is a powerful pancreatic carcinogen in Syrian golden hamsters, with duct carcinomas developing at a high incidence after chronic administration by gavage. The compound exists as a mixture of the cis and trans isomers. The cis isomer has been shown to be a much stronger pancreatic and liver carcinogen in hamsters than is the trans isomer. We studied the morphlogy of pancreatic tumors induced by the cis isomer by light and electron microscopy, and followed the sequential development in a serial sacrifice study. To complement our data, we examined the intracellular sites of binding of [3H]-cis-DMNM and [3H]-trans-DMNM in the target organs by light and electron microscopic autoradiography. Our results suggest that the endoplasmic reticulum of pancreatic acinar cells is the principal site of metabolic activation of both isomers with binding of the cis form being significantly higher. Moreover, our pathogenesis data gives evidence that the pancreatic acinar cell is the origin of the induced duct carcinomas. (no Refs)

64. AUGMENTATION OF CARCINOGENESIS BY N-NITROSOBIS (2-OXOPROPYL) AMINE (NBOP) ADMINISTERED DURING 'S' PHASE IN REGENERATING HAMSTER PANCREAS (MEETING ABSTRACT).

Scarpelli DG, Rao MS, Subbarao V
Department of Pathology, Northwestern University Medical School, Chicago, IL, 60611
Proc Am Assoc Cancer Res; 23:224 1982

The present experiments were undertaken to ascertain the neoplastic potential of acinar cells in hamster pancreas. This was accomplished by administering NBOP to regenerating pancreas when the maximum number of acinar cells are in S phase, as compared to only rare islet and duct cells. Regeneration was induced with ethionine in 30 5-6 week old hamsters. These were divided into 2 groups, which were treated as follows: Group I 30 mg NBOP/kgbwt given at 60 hours of regeneration followed by 10mg/kgbwt/week for 9 weeks; Group II 5 mg NBOP/kgbwt at 60 and 66 hours followed by 10 mg/kgbwt/week for 8 weeks. Three groups of animals consisting of 10 each, with normal pancreas served as controls; Group III received NBOP at doses as scheduled for Group I; Group IV received NBOP at doses as scheduled for Group II; and Group V received 10 mg NBOP/kgbwt/week for 10 weeks. Animals were sacrificed when moribund or at 26-28 weeks. Pancreatic ductal adenocarcinomas were induced in all groups. However, the yield of tumors varied as follows: Grp I, 76%; Grp II, 30%; Grp III, 40%; Grp IV, 20%; Grp V, 27%. In each instance, these were invasive lesions. In many animals neoduct formation was evident in acini. The foregoing is additional support for the notion that under appropriate stimulus (ie), acinar cells can modulate to ductal epithelium and may be involved in the development of ductal adenocarcinoma. (no Refs)

65. COMPARATIVE CARCINOGENICITIES AND TOXICITIES OF N-HYDROXY-N-ACYL-4-AMINOSTILBENES (MEETING ABSTRACT).

Hirose M, Shirai T, Lee MS, King CM
Michigan Cancer Foundation, Detroit, MI, 48201
Proc Am Assoc Cancer Res; 23:232 1982

The abilities of the N-hydroxy-N-formyl-4-aminostilbene (N-OH-FAS), N-hydroxy-N-acetyl-4-aminostilbene (N-OH-AAS), and N-hydroxy-N-propionyl-4-aminostilbene (N-OH-PAS) derivatives of N-hydroxy-N-acyl-4-aminostilbene to induce tumors and unschedule DNA synthesis (UDS) were determined in efforts to relate the metabolic activation of arylhydroxamic acids to their production of adverse biological effects. Hepatocytes obtained from male CD rats were allowed to attach to cover slips for 18 hr prior to treatment with the above compounds (0.1 uM to 1 mM) for 2 hr in the presence of [3H]TdR in serum-free media. On autoradiography of cells treated with N-OH-PAS, the maximum number of grains over the nuclei (36) occurred at a concentration (1 uM) 2 logs lower than with N-OH-FAS or N-OH-AAS. Control cells averaged only 1 grain per nucleus. Groups of 30 male CD rats (100 g) were given intraperitoneal injections of the agents (10 umol/kg bw) in DMSO:trioctanoin twice weekly for 6 weeks. The experiment was terminated 62 weeks after the first injection. The livers of N-OH-PAS-treated animals, at sacrifice, were larger than those of the other groups. Grossly, the number of tumor-bearing rats was 10/29 (N-OH-FAS), 18/29 (N-OH-AAS), 24/28 (N-OH-PAS), and 3/30 (solvent-treated). The number of rats with ear duct tumors were 0, 10, 13, 1; those with pancreatic tumors were 3, 7, 9, 0; and those with liver tumors were 0, 3, 6, 1, in groups given N-OH-FAS, N-OH-AAS, N-OH-PAS or solvent, respectively. (no Refs)

66. EFFECT OF PYRIDOXAL DEFICIENCY ON PANCREATIC DNA DAMAGE AND NODULE INDUCTION BY AZASERINE (MEETING ABSTRACT).

Zurlo J, Roebuck BD, Rutkowski JV, Curphey TJ, Longnecker DS
Department of Pharmacology and Toxicology, Dartmouth Medical School, Hanover, NH, 03755
Proc Am Assoc Cancer Res; 23:264 1982

The purpose of this study was to determine whether the effects of azaserine on pancreas are pyridoxal-dependent. For DNA damage studies, weanling rats were fed a pyridoxal deficient diet containing 4-deoxypyridoxine, a pyridoxal antagonist, until deficiency was evident (10-12 days). They were then injected with azaserine 90 min before sacrifice. The deficient rats inhibited almost no pancreatic DNA damage (as determined by alkaline elution) in response to azaserine when compared to saline-treated rats on control diet. A structurally different pancreatic carcinogen, Ndelta-(N-methyl-N-nitrosocarbamoyl)-L-ornithine, caused DNA damage in both deficient and control groups. Distribution studies with 14C-azaserine showed that the absence of DNA damage was not due to the lack of azaserine transport into the pancreases of deficient animals. In another study, rats were treated with 4-deoxypyridoxine prior to a single azaserine treatment. Rats were killed 4 mo after azaserine administration. There was a significant reduction in the number of atypical acinar cell nodules in antagonist-treated animals compared to controls treated with azaserine but not with the antagonist. These results strongly indicate that azaserine metabolism and carcinogenicity are dependent on pyridoxal. (no Refs)

67. COMPARATIVE METABOLISM OF N-NITROSOBIS(2-OXOPROPYL)AMINE (BOP) IN HAMSTERS AND RATS (MEETING ABSTRACT).

Lawson T, Helgeson AS, Nagel D
Eppley Institute, University of Nebraska Medical Center, Omaha, NE, 68105
Proc Am Assoc Cancer Res; 23:338 1982

BOP induces mostly pancreas tumors in hamsters and colon or prostate tumors in rats. A single dose is effective in hamsters but multiple doses are needed in rats for tumor production. When a dose of BOP, that only produces pancreas tumors (10 mg/kg) was given to hamsters, BOP was concentrated in the pancreas. The max concentrations were 3.7 ng/mg pancreas and 0.6 ng/mg liver. The concentration of N-nitrosomethyl(2-oxopropyl)amine (MOP), the putative proximate carcinogen from BOP, was higher in the pancreas (0.05 ng/mg) than in the liver (0.02 ng/mg). In rats no concentrating effects for BOP or MOP were seen. Rather the metabolism of BOP was directed to the formation of N-nitrosobis(2-hydroxypropyl)amine (BHP) and N-nitroso(2-hydroxypropyl)(2-oxopropyl)amine (HPOP), which are less specific and less carcinogenic than BOP. In rats the max concentrations of BHP and HPOP were 57 and 290 ng/mg, whereas in hamsters they are 18.9 and 20.9 ng/mg. The apparent preferential synthesis of the less carcinogenic metabolites of BOP by rats correlates with the lower carcinogenicity of BOP in rats compared with hamsters. Neither BHP nor HPOP were concentrated in the target tissues when given to hamsters or rats. Also only traces of MOP were found after a single dose of either BHP or HPOP. These results support the idea that MOP is a more proximate carcinogenic form of BOP. (no Refs)

68. PANCREATIC CARCINOMA - A SEX-STEROID RESPONSIVE TUMOUR? (MEETING ABSTRACT).

Greenway BA, Iqbal MJ, Johnson PJ, Williams R
The Liver Unit, King's College Hospital, London SE5, England
Proc Am Soc Clin Oncol; 1:C-23 1982

We analyzed both cytosol and nucleosol from nine specimens of malignant, four of normal, and two of pooled fetal pancreas for estradiol (E2) and androgen receptors, using a ligand binding assay. Results were interpreted by Scatchard analysis. High levels of high affinity E2 receptors were detected in eight specimens of malignant and fetal pancreas (range 157-2769 f mols E2 bound/mg total soluble protein (tsp). No specific androgen binding was detected. Since estrogen sensitive tissues may contain steroid biosynthetic enzymes, we analyzed three specimens of pancreatic tumour and pooled fetal pancreas for aromatase, which converts testosterone (T) to E2, and 5 alpha reductase, which converts T to dihydrotestosterone (DHT). Uterus with high aromatase activity and prostate rich in 5 alpha reductase served as positive controls. Endogenous steroid was removed with charcoal, and the supernatants incubated with NADPH and increasing concentrations of T. End products E2 and DHT were measured by radioimmunoassay. Maximum aromatase activity expressed as p mols E2 bound/mg tsp was 9.73, 16.33, and 2.9 in malignant pancreas, 9.25 in fetal, and 17.86 in uterus. Maximum 5 alpha reductase activity expressed as n mols DHT bound/mg tsp was 0.086, 0.15, and 0.096 in malignant pancreas, 0.06 in fetal, and 0.24 in prostate. The finding of E2 receptors in pancreatic carcinoma may represent reactivation of fetal genes. (no Refs)

69. INFLUENCE OF DIETARY PROTEIN ON BIS(2-OXOPROPYL)NITROSAMINE INDUCED AND SPONTANEOUS TUMORS IN SYRIAN HAMSTERS (MEETING ABSTRACT).

Birt DF, Stepan KR, Pour PM
Eppley Institute for Research in Cancer, University Nebraska Medical, Center Omaha, NE, 68105
Fed Proc; 41(3):358 1982

Treatment of Syrian hamsters with a single injection (10 mg/kg body weight, sc) of bis(2-oxopropyl)nitrosamine (BOP) was previously shown to be selective for pancreatic adenocarcinoma induction. In the present experiment hamsters were fed three levels of dietary casein [low 9% (LP); medium, 18% (MP) and high 36% (HP)] either before (3-8 weeks of age) or after (8 weeks until death) BOP treatment. Animals were given to MP diet at other times and parallel groups were fed by these diet schedules, but not treated with BOP. Pancreatic carcinoma incidence was reduced in females but not in males fed LP diet after BOP treatment [LP, 0% incidence (0/30%) HP, 30% incidence (8/27)]. Lung adenoma incidence was reduced in male hamsters fed the HP diet after BOP (0% incidence) by comparison with those fed LP (17%) or MP (35%) diets at this time. The incidence of spontaneous adenomas was influenced in male hamsters, HP diets fed during weeks 3-8 increased kidney adenomas, and HP diets fed after week 8 increased Cowper's gland adenomas. Longevity was greatest in male hamsters fed the LP diet during weeks 3-7. The effects of dietary protein on tumor incidences in hamsters varies with sex, tumor site and age at which the various casein levels were fed. (no Refs)

70. METABOLISM OF N-NITROSO-2,6-DIMETHYLMORPHOLINE (NNDM) BY THE VARIOUS COMPONENT CELLS OF HAMSTER PANCREAS (MEETING ABSTRACT).

Scarpelli DG, Rao MS, Kokkinakis D, Hollenberg P
Department of Pathology, Northwestern University Medical School, Chicago, IL, 60611
Fed Proc; 41(3):927 1982

It has been shown that hamster pancreas contains enzymes which activate the pancreatic carcinogens NNDM and N-nitrosobis(2-oxopropyl)amine (NBOP) to forms which are mutagenic for Salmonella typhimurium. The metabolism of [3H]NNDM by S-9 and microsomal fraction of whole pancreas (WP) and acinar cells (AC) and S-9 of islets (IC) isolated from normal and 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)-treated pancreas is reported here. Metabolic capacity of duct cells was determined by incubation of pancreas slices in medium containing NNDM in the presence of [3H]-thymidine with and without hydroxyurea to assess unscheduled DNA synthesis (repair). HPLC (high pressure liquid chromatography) analysis showed that S-9, of WP, AC and IC metabolize NNDM to the following compounds in descending order of concentration: HPOP greater than NBOP greater than BHP; NBOP greater than HPOP greater than BHP: and NBOP greater than HPOP greater than BHP. Pretreatment with TCDD increased total metabolism in all circumstances (WP,141%; AC,110% and IC,85%). Microsomes of WP and AC produced the sequence NBOP greater than BHP greater than HPOP. Metabolism by S-9 and microsomes of pancreas was approximately 1/20 of those isolated from liver. In contrast to pancreas, the predominant metabolite produced by liver was HPOP. Unschedules DNA synthesis in nuclei of duct epithelium indicates that these cells are capable of metabolizing NNDM to an active form. (no Refs)

71. A FAMILIAL AGGREGATION OF PANCREATIC CANCER: AN IN VITRO STUDY (MEETING ABSTRACT).

Danes BS, Lynch HT
Cornell University Medical College, New York, NY
Proc Am Assoc Cancer Res; 23:152 1982

Solid clues for the epidemiology of pancreatic cancer have been exceedingly limited. Although familial aggregations of pancreatic cancer have been observed, genetic versus environmental roles have not been clarified. Biomarker research harbors the potential for identifying members at increased cancer risk due to their genotype within such aggregates. In vitro research has been based on the hypothesis that normal cells from a skin biopsy when grown in culture show in vitro expressions of cancer prone genes; one of these is alterations in chromosome complement number. This hypothesis was tested in studies of such a family. Diploidy has been a constant feature of such cultures derived from normals (without a family cancer history). Hyperdiploidy with the exception of tetraploidy has rarely been observed. Cultures established from 17 family members could be divided into two groups: 1) with and 2) without hyperdiploidy. Cultures from 9 family members, 7 family members by-marriage and 10 non-family members showed normal tetraploidy and no other hyperdiploidy. The other 8 family members had increased hyperdiploidy exclusive of normal tetraploidy. This was the first demonstration of an in vitro abnormality showing vertical transmission in 2 consecutive generations in a familial pancreatic cancer aggregate. An extension of such an in vitro approach to other such clusters may help to clarify factors in the etiology of pancreatic cancer. (no Refs)

72. SEPARATION AND CHARACTERIZATION OF NEOPLASTIC CELL SUBPOPULATIONS OF A TRANSPLANTABLE RAT PANCREATIC ACINAR CARCINOMA.

Becich MJ, Reddy JK

(c/o Reddy) Dept. Pathology, Northwestern Univ. Medical Sch., 303 East Chicago Ave., Chicago, IL, 60611

Cancer Res; 42(9):3729-3740 1982

The transplantable pancreatic acinar carcinoma established in F344 rats demonstrates heterogeneity of cytodifferentiation with cell types ranging from those containing no zymogen granules to cells with mature zymogen differentiation. Two relatively homogeneous subpopulations of cells were isolated by isopyknic Percoll gradient centrifugation from the heterogeneous cell population of this tumor. The subpopulation obtained at a density of 1.0987 g/ml was designated the granule-enriched fraction (GEF) and contained morphologically differentiated cells with abundant mature zymogen granules. The other subpopulation, obtained at a density of 1.0789 g/ml, consisted of poorly differentiated cells lacking zymogen maturation and was thus termed the granule-deficient fraction (GDF). In both fractions, greater than 97% of the cells were viable and maintained linear rates of [3H]leucine and [3H]thymidine incorporation into protein and DNA for up to 3 hr following isolation. Twenty percent of the cells in GDF subpopulation and 12% of the cells in GEF subpopulation synthesize DNA. Distinct differences in nuclear:cytoplasmic ratio, secretory granule content, and degree of polarity were found between GDF and GEF. The GEF subpopulation contained high levels of amylase and lipase, while the GDF subpopulation displayed very low levels of these enzymes. Both subpopulations produced tumors when injected sc into F344 rats. Concanavalin A (Con A) receptors were found on pancreatic carcinoma cells regardless of the extent of cytodifferentiation in contrast to normal pancreatic embryogenesis, in which Con A receptors are discerned only in acinar cells containing mature secretory granules. This finding suggests either that the neoplastic transformation results in altered genetic expression or that pancreatic carcinoma arises from dedifferentiation of mature acinar cells which normally possess Con A receptors. (52 Refs)

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NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. ASBESTOS CARCINOGENESIS: ASBESTOS INTERACTIONS AND EPITHELIAL LESIONS IN CULTURED HUMAN TRACHEOBRONCHIAL TISSUES AND CELLS.
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Environmental Mutagen Information Center, Oak Ridge Natl. Lab., Oak Ridge, TN, 37830
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NEW ONCOLOGY OVERVIEWS
ON CARCINOGENESIS

The following are titles of retrospective bibliographies that contain 100-500 selected abstracts of recent cancer research publications on carcinogenesis topics. Additional Oncology Overview titles are also available for the Cancer Diagnosis and Therapy Series and the Cancer Virology/Immunology/Biology Series; these titles will be announced on separate forms for convenient ordering.

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